

ANALOGY AND METAPHOR IN THE DESIGN
OF VISUAL ARTIFACTS FOR BIOLOGY.
THE EXAMPLE OF THE MACHINE DE LEJEUNE.

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Analogy and metaphor in the design of visual artifacts for biology. The example of the Machine de Lejeune.

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Abstract

The PhD work focuses on the design of visual artifacts for scientific research in the domain of biology, in laboratory environments and in the process of scientific discovery. The dissertation is presented as an epistemological study of information and communication design, collecting input from different fields of knowledge, from biochemistry to Human-Computer Interaction and design theories, from the sociology of scientific practice to semiotics and philosophy of science. The goal is to enrich the cultural background available to information and communication design with the experience and knowledge accumulated also by other disciplines.

The choice of the domain of biology is driven by the artifact taken as an example of a significant application of analogy for visual communication and scientific explanation: the “Machine de Lejeune” (1978), a visual artifact developed by Jérôme Lejeune, who drew a visual analogy with a fictional mechanical calculator to describe the metabolism of a human nervous cell. Strong attention is given to the concepts of metaphor and analogy, and how these rhetorical devices become an integral part of scientific endeavors. These rhetorical devices are mentioned by literature in Human-Computer Interaction as privileged instruments for creating conceptual models, the foundation of meaningful communication design artifacts. The logical function of analogy and metaphor of mapping two domains is meant to lead the readers to a better understanding of the functioning of an information system. However, literature in the design field seldom provides descriptions of analogies and metaphors which can be directly applied and controlled in the design of visual

artifacts. The dissertation highlights the knowledge in literature available for analyzing these logical devices.

The dissertation also provides guidelines on how to identify and manage the design issues considered most challenging for the designer who approaches the analysis and production of visual artifacts for biology and those which include analogies and metaphors.

Lejeune developed the Machine as a communication device for specific research and dialogical reasons. The analogy he embedded in his scientific model and representation allows the specialists to access complex biochemical information and to infer divergent data patterns due to metabolic conditions in Trisomy 21. The Machine is an unprecedented visual representation in the field due to its conceptual and graphic premises. The dissertation benefits from this example by putting it in relation to multidisciplinary literature. The collected knowledge supports the designers in understanding the facets of the design problem while creating visual artifacts for scientific explanation in biology: in understanding the logical implications of analogy, metaphor and models for communication purposes; in getting acquainted with the domains to put into relation through the visual analogy; in stating which is the main hypothesis and vision driving the representation; in determining the way the hypothesis is rendered visually and which parts are purposefully left out; in elaborating the dialogical role the scientific équipe should attribute the visual artifact during laboratory practice.

By supplying aptly crafted visual artifacts, designers can support scientific researchers in their laboratory work and also make a significant contribution to welfare and society as a whole.

KEYWORDS

Information design, metaphor, analogy, visual analogy, scientific models, Machine de Lejeune

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1.

The analogy of a Machine

1.1.

Information accessibility in the quest for scientific discovery

Information accessibility is at the core of visual communication design (Bandini Buti, 2019, p. 7; Falcinelli et al., 2014; Perondi, 2012, p. 17): whatever we produce, whichever communication artifact we make, the goal as information designers is to allow somebody to understand context and domain, to make meaningful connections between information, to infer and use elements of knowledge by hooking the readers' reasoning process to a visual representation.

Either mundane, or safety-critical, or scientifically relevant, everyday tasks are deeply influenced by how people understand the knowledge domain and actively reason on it. Daily, people struggle even to find the ticket machine in an underground parking lot without proper directions in the environment. And if we find it, now we face the issue of understanding what even is the procedure to free our car from the parking lot: do I pay in advance and hope the parking bar rises when my car approaches it? Do I need to digit my car's license plate somewhere, or perhaps the slot number where my car currently sits?

Do I even remember these data at hand? Should I have marked the entrance time to the lot, or did some automatic system mark my license plate numbers when I entered the parking lot?

Now, try to imagine finding the cause of the symptoms associated with Trisomy 21, the genetic condition commonly known as Down's Syndrome. Where does a biology équipe even start from? They cannot even see the molecules they are working with, for obvious reasons. How can they create meaningful connections within the biology domain since it is so complex and largely based on raw numeric data to analyze? How do they find the cause of symptoms, if they cannot rebuild the chain of reactions making up the human metabolism?

For this exact purpose of self-help in the process of discovery, science for centuries developed visual representations. Representations born out of sheer need to have something to grasp on, out of inquisitiveness, out of truly remarkable views and ideas. Information and communication designers can contribute significantly to the ideation of representations and provide meaningful support in this journey.

This dissertation is presented as an epistemological study of information and communication design, with a particular focus on metaphor and analogy. These rhetorical devices recur in the design literature as important tools, appropriate to the work of the information and communication designer. However, metaphor, analogy and their related logic-rhetorical concepts are systematically neglected in detail by the literature in the design field.

The dissertation ranges across more or less contiguous fields of knowledge, from biochemistry to Human-Computer Interaction and design theories, from the sociology of scientific practice to semiotics and philosophy of science. The epistemological intent of the PhD work is twofold: to give visibility to design as a participant actor and active interlocutor in the scientific work of these disciplines; to bring to the design community an *outside* perspective that enriches the cultural background

available to the information and communication design with the experience and knowledge accumulated by these other disciplines.

The overall goal then is not to provide a theory on the design of visual artifacts for scientific use but to highlight which scientific actors and topics are found by facing this design activity. The scope of the enquiry then is more horizontal, trans-disciplinary, with more in-depth incursions into the key areas that are encompassed by the example visual artifact, namely the Machine the Lejeune. The choice of the areas of study in scope is thus emergent from the case study. Within each area explored the methodological and design inputs that are deemed most interesting for information and communication design are collected towards a final synthesis. Strong attention is paid to the examination of the concepts of metaphor and analogy, precisely to fill those gaps in the design literature mentioned earlier.

Following this figurative journey into different disciplinary domains, a pragmatic summary is proposed, enlisting the design issues considered most challenging for the designer who approaches the study and production of visual artifacts for biology, and especially visual artifacts in general that include analogies and metaphors. In closing, a series of pragmatic and scientific proposals are described for the continuation of work on the Machine, toward the development of a possible digital variant of the artifact.

Overall, the research presented in this volume finds its place in the field of visual communication design applied to the visualization of scientific models in biology. More specifically, the object of focus is the graphical representation of a biochemical model of the metabolism of a human cell. The example case discussed is of a specific visual artifact, “La Machine de Lejeune” (Figure 1) which was designed by Jérôme Lejeune, the geneticist who contributed to the discovery of Trisomy 21. Lejeune presented the artifact as a poster in 1978 at the *Well-being of*

mankind and genetics conference (J. Lejeune, 1980) in Moscow. On that occasion, Lejeune himself states:

Here again the complexity is bewildering and to get an impression of it I tried to figure out a “pascalian machine” which could roughly simulate the intricacies of the chemical pathways. In this artistic view (if I can say so), only the pathways well established enough to be found in current textbooks have been drawn; most of them incompletely. This is to say that the true machinery is much more sophisticated than this primitive oversimplification. Nevertheless, the analogy can be of some heuristic use. (J. Lejeune, 1980)

Lejeune in this artifact, by making a visual analogy with a pseudo-pascalian machine, represents the chemical reactions happening inside the neurons (J. Lejeune, 1981b), as if the metabolism itself was a mechanical machine whose metabolites are the gears. The general aim of the artifact is to allow the biochemistry researcher to report the known genetic diseases known on the scheme and to state the *dynamic* effect of each disturbance. Indeed the motion of the gears reconstructs analogically the chain of reactions operated by the human *calculator*. Lejeune was convinced that finding where anomalies occur in the Machine was the key to understanding the divergent development determined by Trisomy 21 (J. Lejeune, 1980).

The objective of his efforts was in perspective to search for a cure for Trisomy 21 so that the way towards curing all the other genetic conditions could be opened. The interest in the metabolic mechanisms leading to disorders in intelligence and functioning of people is indeed functional to this vision (C. Lejeune, 2008, p. 25). Notably, the research interest of the model is to provide clues not exclusively for genetic conditions, but also to other conditions like psychotic syndromes for example, which might or might not be determined by a chromosomal anomaly but which can be linked to defined metabolic disorders

La Machine de Lejeune

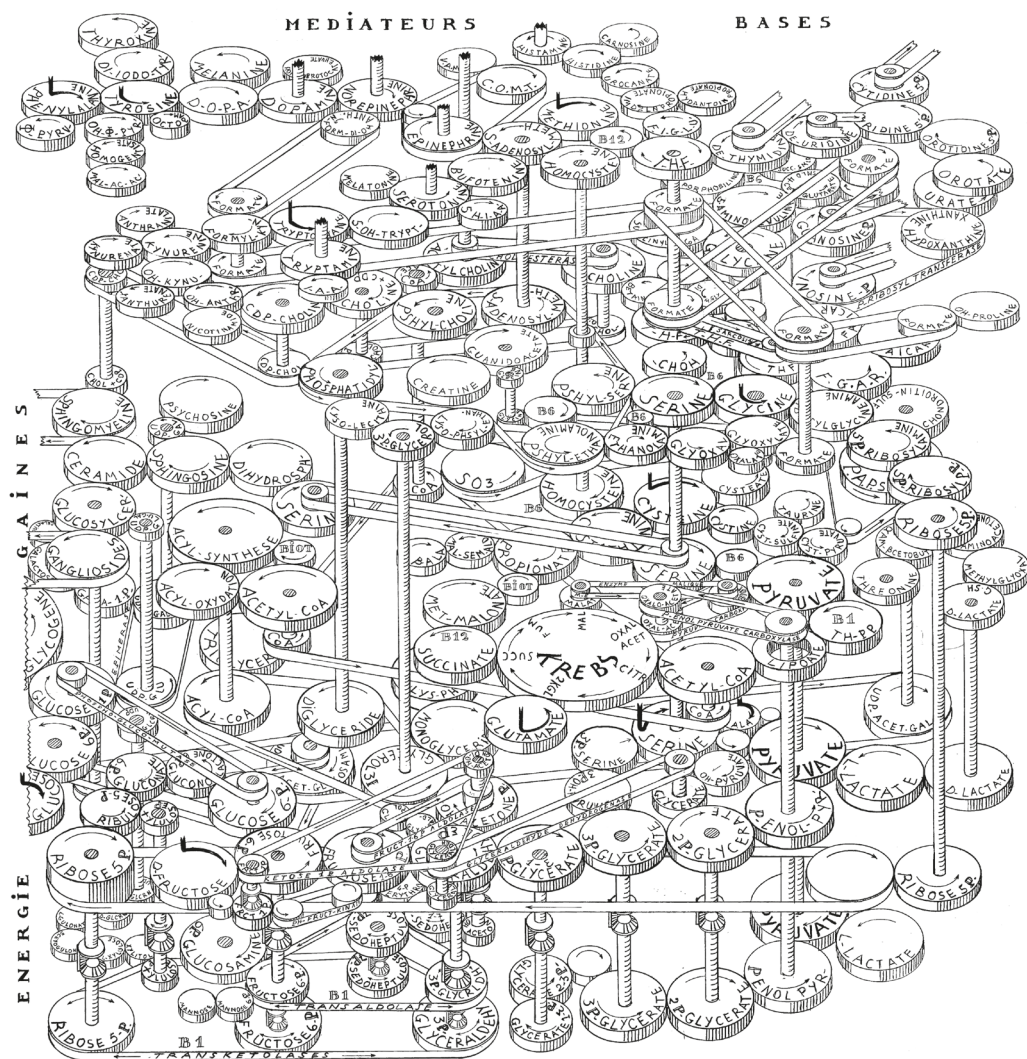


Figure 1

The original poster of La Machine de Lejeune.

Drawing by Jérôme Lejeune, obtained thanks to courtesy of Mme Birthe Lejeune and used with her kind permission.

(J. Lejeune, 1990). The mindset and the heuristic approach which leads Lejeune allows him to range to various avenues of research, always related to the biochemistry of the metabolism, but concerning different pathologies and conditions. The importance he gives to mapping the human metabolism is functional to find treatment for a variety of problems which he calls “les maladies chimiques”, or “the chemical illnesses”.

It is therefore clear that in this case, as in many others in the history of science, scientists use the logical mechanism of analogy as an expedient to formulate hypotheses, even make up scientific models, or use analogy for heuristic purposes. Hesse (1980) suggests a strong interaction between analogy and the scientific model, in which the one informs the other and vice versa, in contrast with a more rigid separation between scientific model and analogy as Duhem suggested (Hesse, 1980, pp. 45–79). Scientists indeed over the centuries made use of analogy as a way to define models and theories. Salvi (2014, pp. 31–32) provides a quick list of well-known examples: Johannes Kepler (1571–1630) tried to explain the motion of planets through an analogy with the motion caused by magnets on iron; Isaac Newton (1642–1727) reached his definition of the corpuscular nature of light with the help of an analogy with the trajectory of tennis balls when they are hit so as to have a spin, curving as they travel through the air; Robert Hooke (1635–1703) illustrates meteorological phenomena through an analogy of experiments with pneumatic pump, or the lymph circulation in plants with a model of capillarity, or the formation of water springs with the model of elasticity; Charles-Augustin de Coulomb (1736–1806) investigated magnetic forces through analogies with electrostatic force and gravity; Nicolas Léonard Sadi Carnot (1796–1832) proposed the metaphor of heat as a sort of fluid travelling from a body to another. He is partially mistaken, missing the first law of thermodynamics; James Clerk Maxwell (1831–1879) starting from the model of the lines of force of Faraday uses an analogy

with laws of hydrodynamics to propose his model for thin pipes traversed by an incompressible fluid (the ether). Undoubtedly, analogy and metaphors are part of scientific thinking in practice. Some models more than others used visual representations as a means to reach a more formal theory, let us think for example of Charles Darwin's "Coral of Life" (1837) or the "Planetary Atomic Model" by Rutherford (1911), with a variety of example representations on biological evolution (Archibald, 2014).

By implicitly sharing this view on the usefulness of analogy, Lejeune tries to map and draw the causes of symptoms related to Trisomy 21, in an attempt to help himself, and whoever wants to accept this intellectual and scientific challenge, to reach the ambitious goal of curing through metabolic therapies the symptoms caused by Trisomy 21. By making tangible (visible) the "solid reasoning within himself" (Moxon, 1683, p. 6), Lejeune touches the core of what we can define as information design: the attempt to broaden the access to a complex domain by defining and visualizing the information necessary, sufficient and comprehensible to the people at various moments, performing creative synthesis of complex issues while encompassing specific methods and less extemporary approaches to creativity (Bandini Buti, 2019, pp. 59–60). The Machine is an act of design in and of itself.

Due to their key role in this dissertation, the concepts of metaphor and analogy are quickly introduced hereafter, while their definition and implications are discussed in detail in Chapter 4.3. It is not simple to discern those two concepts in a clear-cut way, since they interplay and overlap in terms of logic or linguistics, depending on the angle the scholars study them. However, to simplify, in this dissertation we can keep them distinct by describing the analogy as the cognitive activity of the reader in defining a mapping between the relations of elements of one domain and the relations of elements of a second domain. On the other hand, we can describe metaphor as the expression on the communication plane (either written, graphic, etc) which

suggests relations to identify and explore through analogical reasoning. It is evident the interplay between the cognitive activities of identifying and communicating the observed or hypothesized relations: without having any clue or reason to posit an analogical relation between two domains, the sign-producer cannot utter a meaningful metaphor; on the other hand, without adequate means of expression and communication (linguistic, graphical, etc) a hypothesized or objective analogy cannot be described by the sign-producer in ways that make it have impact on the discourse, or that make any sense to the reader. The efficacy of communication of analogies and metaphors is peculiarly important given their fundamental purpose: to be logical devices that support the reader to create new knowledge or to strengthen connections between elements of knowledge, effectively making information more accessible. This purpose is of course proper to those analogies and metaphors which are not mere embellishments or sterile figures of speech.

To better clarify the concepts of analogy and metaphor, let us make a quick and simplistic example on the graphic artifact of the Machine de Lejeune. Lejeune's hypotheses include the fact that the excess of a chromosome in people with Trisomy leads the metabolome (the whole collection of molecules created and transformed within the metabolism) of these people to be "out of balance". So if we say that some metabolic pathways are "slowed down", we are uttering a metaphor between biological entities and an unspecified something that possesses mechanical properties (or more in general properties of the motion of bodies, belonging to physics and mathematics). Lejeune builds upon and expands via analogical reasoning the concept of *imbalance* by envisioning an overarching metaphor, for which the human metabolome is a clockwork machine, whose components are made to be always perfectly synchronized, to conceptually seek where the Machine does not run as intended. That's where analogical reasoning comes into play: if we now have this machine, which other relations between the

elements of knowledge of biology can be found in an analogue way in the domain of mechanics? A metabolism is made of reactions operated by cells on molecules, whose concentration is converted along the chain of reactions, as much as a machine is made out of components converting motion along their chain. What if the metabolites behave as the “gears” in the Machine? Furthermore, in biology reactions do not happen randomly but they are “grouped” in chemical pathways, as much as in a machine all the gears are not randomly connected, but they are chained contiguously in groups to serve specific functions. And so on. From the general metaphor of metabolome as a machine, metabolites as gears and so on, a multitude of hypotheses and inferences can be made through analogical reasoning on the two domains of biology and mechanics. Several layers of reasoning and considerations are condensed within the visual artifact of the Machine de Lejeune, which are discussed more in detail throughout Chapter 2.

Literature in Human-Computer Interaction (HCI) provides further context around the use of metaphors and analogies as design tools. In the design of interactive systems, the activity performed by designers to set up conceptual models through the use of effective metaphors is recognized as a central theme in the expansion of the HCI research discipline (Blackwell, 2006). The discourse applies to information design as well, of course, since conceptual models are a way to structure and propose information, even before enticing interactivity through digital media. Blackwell (2006) provides a precise overview of the topic within the HCI research community: the designer-researchers in HCI employ their skills and insights to see new analogies with the aim to construct effective metaphors, while at the same time drawing from theoretical research to guide themselves in the choice of the best sets of correspondences. In this process, there is a dose of creative authorship as well, not just technical competence. Designers can critically reflect and employ tactics to set up the metaphor rhetorical device in a meaningful way, under

the pressure of research needs or market requirements. While doing so, they can contribute further to the definition of the design discipline through a process of reification, that is to make abstract concepts more concrete by either elaborating techniques and devices to be reused, or developing specific products (e.g. software interfaces) embedding those concepts. In the HCI design field indeed the outputs of the work are the *products*, whether research prototypes or commercial products, always blending and embedding technical knowledge into theoretical one. Metaphors are part of the conceptual toolset of the designer, and therefore they are embedded in the visual artifacts product of their work of design. Usually, this product of design must then withstand the test of the market and possibly be adopted by a vast base of users. This is when the feedback loop of the efficacy of metaphors becomes disturbed: normally the metaphors and the artifacts themselves are produced more to solve practical engineering problems and less to provide clear feedback on the metaphor itself, as formal scientific testing would do. Given this natural setup of the context of the discipline, an alternative strategy which the HCI research community practices is to collect scientific (and multidisciplinary) evidence and theories and retrospectively interpret them to answer design questions, in an attempt to influence product design through the influence on designers. The analysis and use of metaphors in the context of the design of interactive systems go in the direction of finding ways to develop appropriate metaphors in use rather than solving problems through theoretical analysis alone.

This dissertation is in line with the design research and practice in HCI summarized from Blackwell. The various chapters collect and comment on inputs from various disciplines to provide guidelines where these indications converge. Of particular interest is the unique blend of the metaphorical representation of the example artifact of the Machine de Lejeune, the domain of biochemistry and the communicative purpose of the example artifact. This blend provides indeed varied and in-depth

accounts of the way a communication artifact shapes and incorporates reflections on metaphors and analogies from various disciplines towards information design. The dissertation and resulting set of guidelines proceeds deductively from the study of the model of the Machine and abductively from the multidisciplinary literature in a continuous loop, in an attempt to provide indications for future inductive investigations proper to information design.

What we can argue through the lens of the example of the Machine the Lejeune is that the creative endeavour of elaborating meaningful metaphors to embed in visual artifacts is shared throughout the scientific community, it is not solely part of the design ontology. The Machine itself is just an instance of the many analogical or metaphorical representations in the history of science, and therefore a sign of a way of thinking more than a dedicated praxis of a discipline. The main difference between scientific practice (in biology in this case) and the design practice lies more in the output of the process of reification. As also commented in Chapter 4.2, in the biology laboratory discussions the artifacts are prepared to spark conversation hopefully leading to fertile hypotheses and conclusions, or to prepare the evidence for publication. Design applications can serve the same purpose but also they are often oriented to a consumer market, with all the limitations, opportunities and paradigm shifts demanded by this context. User Interfaces for Windows® and macOS® operating systems are some of the most known examples, which indeed make use of metaphors such as the “desktop”. This topic is discussed further in Chapter 3.

By drawing the Machine visual artifact, and therefore by making an act of *writing* (Lussu, 2003, pp. 11–37), Lejeune integrates his medical and biochemical knowledge within a “simplistic” mechanical model, with the aim of understanding where this pseudo-pascalian machine does not work “properly”, and consequently proceeding with appropriate therapies for the treatment of the metabolic syndrome:

Over such a scheme, we can superimpose the genetic blockages known to provoke mental deficiency. As expected by the analogy with computers, we discover that failures do happen in parts of the machinery [...] (J. Lejeune, 1980)

It is evident that while pursuing this objective, Lejeune moves back and forth between the first domain (biochemistry) and the second one (mechanics) in a continuous loop, in an attempt to exploit the strengths of analogical reasoning. One of the attempts of this dissertation is to provide insights for the design community on how to manage the complex interplay between language, logic, and science implied by the use of models (including metaphors and analogies) in science, as a way to build a bridge between science and humanities, as design can do. This attempt is perfectly described by the philosopher Max Black, whom I would like to quote fully;

If I have been on the right track in my diagnosis of the part played in scientific method by models and archetypes, some interesting consequences follow for the relations between the sciences and the humanities. All intellectual pursuits, however different their aims and methods, rely firmly upon such exercises of the imagination as I have been recalling. Similar archetypes may play their parts in different disciplines; a sociologist's pattern of thought may also be the key to understanding a novel. So perhaps those interested in excavating the presuppositions and latent archetypes of scientists may have something to learn from the industry of literary critics. When the understanding of scientific models and archetypes comes to be regarded as a reputable part of scientific culture, the gap between the sciences and the humanities will have been partly filled. For exercise of the imagination, with all its promise and its dangers, provides a common ground. If I have so much emphasized the importance of scientific models and archetypes, it is because of a conviction that the imaginative aspects

of scientific thought have in the past been too much neglected. For science, like the humanities, like literature, is an affair of the imagination. (Black, 1962, pp. 242–243)

Lejeune was a great communicator, both on scientific subjects and on more human and ethical topics. His writings and speeches are rich in metaphors and analogies which are accessible to audiences with just some introductory knowledge. By no mistake, an artifact like the Machine was conceived by such a personality. As his daughter remembers (C. Lejeune, 2008, p. 34–35), Lejeune liked to make people understand, for him knowledge was not an attribute of power, but a way of sharing. He was less used to explaining, and more to narrate. Who knew him (Le Méné, 2008, p. 17) reminds his peculiar trait of trying to stimulate, to elegantly wake the intelligence of the interlocutor whoever he or she was, using communication to elevate the interlocutor's understanding to his own in the attempt to bridge the inevitable gap of knowledge between the two. He was also a man of varied interests (C. Lejeune, 2008, pp. 34–35), he read Greek and Latin, and classic literature, he enjoyed painting and music, philosophy and theology, and he was well versed in ancient history. From a vivid mind open to what culture, arts and technology can offer, surely good narration and significant analogies can come to life.

Given the important role that the graphic visualization of the Machine de Lejeune can play in the process of scientific discovery, the study of this artifact and its context of use is of great interest to the research in information design. The Machine is indeed a visual and communicative logical device, which can play a substantial role in the advancement of the research on Trisomy 21 or other genetic conditions.

The Machine is an unprecedented visual representation in the field of biochemistry, due to its conceptual and graphical premises. It is also noticeably and perceptively different from other metabolism representation systems currently in

use in biochemistry. Lejeune developed it for specific research and communication reasons, as much as ethical ones. Some of these reasons, first and foremost for being against abortion, had him criticized by the scientific community beyond the scientific arguments he brought to the debate. Reasons which also cost him a Nobel prize, in his opinion (C. Lejeune, 2008, p. 25). Nevertheless, these reasons shaped his way of conceiving the scientific problem into the particular scientific and visual model of the Machine. Avenues of research in biochemistry, especially cytogenetics, are still based on the premises of the model and Lejeune's research in general. Indeed, one of the arguments of this dissertation is that the vision of the scientist is intrinsically and inevitably linked to the way he or she organizes knowledge through the proposed model. The model becomes the message of this vision.

These matters, added to the scarce notoriety of this artifact—which was presented at some conferences by Lejeune in the '70s and then archived without undergoing substantial diffusion until the present days—made it important to investigate further on the Machine unexpressed potential from the information design standpoint.

Approaching such a complex topic from the design perspective, even though the natural domain of development of the artifact is biochemistry, results from the opportunity to collect first-hand insights on the artifact by specialized researchers in the domain, and from a precise vision of the role of design in relation to the society. Quoting and extending from Flusser (2003, pp. 63–67), designers should acknowledge the responsibility of improving or being a detriment to the well-being of the society, to avoid total discharge of accountability between decision-makers, producers (designers) and users (or citizens, if we will). This responsibility forms by questioning what the design brings into the society, (1) without blindly relying on the direction of authorities (religious, political or moral that are, whose competencies can be biased or not credible) and interpreting science, (2)

acknowledging the impossibility to produce anything new alone, and to rely on team effort, cooperation and shared responsibility, which is founded on a common moral or ethical vision for the joint activity and not on the shift of responsibility, and (3) taking into consideration the implications of the choices made during the project phase, refraining from relying solely on an external authority for judging the use of the outputs of the design.

It is worth reflecting in depth on these three basic dimensions of responsibility in design because regardless of the level of awareness of the designer about them, they come into play in each project. For as much as the designer might not want to identify their effort with specific ideologies, ethical stances or visions, working in communication and information design makes this somewhat unavoidable. The conscious decision to communicate or not communicate facts, ideas and visions through representations, inevitably positions the designer in some way in the debate. However, this is precisely what makes design an active phenomenon in society, capable of supporting initiatives or directing efforts towards brighter futures. Applying this sense of responsibility allows design to take part in the debate on the great themes of contemporary society, in an independent, conscious and critical way, but that can never be apolitical or amoral. Not exerting and discussing this responsibility condemns design to the margin of the debate and to the low relevance of its impact.

The research presented in this volume is conducted in collaboration with the Laboratorio di Genomica, Dipartimento di Scienze Biomediche e Neuromotorie (DIBINEM), Università di Bologna, directed by Prof. Pierluigi Strippoli. The collaboration allows the creation of a unique real-life case study, in which the shared work between medical-biochemical researchers and designers can make a significant contribution not only to the academic debate but also to welfare and society as a whole.

Before discussing about the visual artifact of the Machine, it is worth mentioning in brief some biography of its author

(Institut Jérôme Lejeune, n.d.; Le Méné, 2008; J. Lejeune, 2002, pp. 137–138), to get a better idea of the historical and scientific context around Jérôme Lejeune and his work. Jérôme Lejeune (Figure 2) was born in 1926 in Montrouge, near Paris. He became Doctor in medicine and researcher, and in 1952 he joined the team of Professor Raymond Turpin at Saint-Louis Hospital (Paris), where he started his studies on the condition known at the time as “mongolism” (the Down’s Syndrome). In 1958 he and his colleagues Marthe Gautier and Raymond Turpin discovered the genetic causes of the syndrome, the Trisomy 21, linking for the first time intellectual disability with a chromosomal abnormality. This discovery earned him the Kennedy Prize in 1962, awarded to him directly by USA President John F. Kennedy. After this first breakthrough discovery, he started working with a number of colleagues in founding what we today call the discipline of cytogenetics. In 1964, he became the first Professor of Fundamental Genetics at the Faculty of Medicine in Paris. About the same time, he was appointed as international expert for France on atomic radiation at the United Nations, due to his works on the effect of radiation on men. In 1969 he was awarded the William Allen Memorial Award (one of the highest honors in genetics worldwide) for his work on chromosomal diseases, and in 1993 he received the Griffuel Prize for his work on chromosomal abnormalities in cancer. Lejeune has been very active in the public debate since the ’70s, giving talks and interviews worldwide, taking clear positions against abortion. In 1974 he was nominated member to the Pontifical Academy of Sciences by Pope Paul VI, and in 1981 he also participated in the works of the Academy on the consequences of the use of atomic weapons on the survival and health of humankind. He went on a mission with eminent colleagues to speak with Russian Prime Minister Brežnev against atomic warfare. In 1981, he was elected to the French Academy of Moral and Political Sciences. In 1994, he became the first President of the Pontifical Academy for Life created by Pope John-Paul II. He died on April 3, 1994.

Lejeune's life, work, ideas and ethical positions contributed to the making of one of the most interesting models for biochemistry in the last century. Lejeune indeed did not focus solely on research and cure (Casini, 2008b, p. 10), but following his vocation he publicly debated through messages to political authorities in France, television programs, public trials on sensitive topics (such as the famous one in Maryville, Tennessee, USA, in 1989, debating on *in vitro* conception), public writings and books. He was a vocal animator of a pro-life cultural stance, in years when these topics took a lot of space on public media and in specialized avenues.

For his positions he was deemed controversial by the scientific community of his time, often criticized despite the scientific arguments he brought in the debate (Colombo, 2002, pp. 6–14), but the extent of his contribution to the field of medicine and biochemistry is indisputable. Lejeune's fruitfulness of thought (Le Méné, 2008, p. 18) was the exact opposite of the one of a wise man well comfortable in his ivory tower. He left an outstanding legacy in many of the topics which made people passionate and impacted their lives significantly over the last century, both in theory and in practice, as much as on the scientific and human side. He surely left a mark in a century where disciplines tended to isolate themselves. He was a specialist but with the talent of connecting people and thoughts across disciplines.

The contents of this dissertation are organized as follows:

- ◇ CHAPTER 1. THE ANALOGY OF A MACHINE
Introduction chapter, with subchapters introducing the topic of information accessibility, introduction to the genome research project in collaboration, summary of research questions, introduction to the themes behind the Machine de Lejeune and metabolome visualization.
- ◇ CHAPTER 2. LEJEUNE, SCIENTIFIC THINKING
Chapter collecting Lejeune's papers, illustrating the whole topic of the Machine. It includes subchapters discussing the

foundations of Lejeune's search for a *heuristic hypothesis*, the ethical reasons moving Lejeune's research and for the adoption of a heuristic method, metaphors and analogies which Lejeune published and which introduce the biochemical and medical topics, and subchapters that focus directly on the artifact of the Machine at increasing levels of detail.

- ◇ CHAPTER 3. RHETORICAL DEVICES IN DESIGN
chapter collecting literature in information and interaction design which discusses the production of design artifacts for conceptual modelling and involving metaphors and analogies.
- ◇ CHAPTER 4. UNIVERSES BEHIND A MACHINE: ANALOGY, REPRESENTATION AND SCIENTIFIC PRACTICE
Chapter collecting literature regarding the use of representation in scientific practice, with a focus on metaphor, analogy and models in science.
- ◇ CHAPTER 5. IMPLICATIONS FOR THE DESIGN OF VISUAL ARTIFACTS IN SCIENCE
Chapter that synthesizes literature in design, Lejeune's papers (and the Machine), and the literature on the use of representation and rhetorical devices in scientific practice, to give guidelines on factors relevant to information design for the design and use in scientific contexts of visual artifacts including analogy.
- ◇ CHAPTER 6. SUGGESTIONS FOR FURTHER RESEARCH
Chapter collecting future perspectives for the shared work with the Laboratory of Genomics, including the work that could not be tackled during the doctoral timeframe. In addition, it is proposed the rationale for the future software development of a digital model of the Machine.



Figure 2

Photograph of Jérôme Lejeune.

Retrieved September 16, 2023, from https://commons.wikimedia.org/wiki/File:J%C3%A9r%C3%B4me_Lejeune.TIF. Fondation Jérôme Lejeune, CC BY-SA 3.0 <<https://creativecommons.org/licenses/by-sa/3.0/>>, via Wikimedia Commons

1.2.

An ongoing research into the causes of Trisomy 21

The work presented in this volume stems from the collaboration with the Laboratory of Genomics at the DIBINEM Department at the University of Bologna. The laboratory is currently led by Dr. Pierluigi Strippoli, Associate Professor of Applied Biology, with the stable collaboration of Lorenza Vitale, Maria Chiara Pelleri, Maria Caracausi, Allison Piovesan, researchers in Molecular Biology, Computational Biology and Genomics.

After years of studies on the human genome and human chromosome 21 by using bioinformatic, genomic and post-genomic analysis methods, in 2013 the laboratory research group led by Dr. Strippoli started *Progetto Genoma 21*: the project pursues the systematic study of Trisomy 21 by integrating clinical, biochemical, genetic and bioinformatic data with the aim of developing unprecedented therapeutic practices for the disabilities that are currently associated with the Down Syndrome.

A quick introduction to the characteristics of Down Syndrome, summarized from Lejeune (J. Lejeune, 1959), is useful to envision the clinical context and the illnesses that the people who are affected by the condition face every day. People with Down Syndrome have very distinctive appearances, due to evident features of the body such as a short stature and stocky appearance, a round head with a flattened profile, a nape that is also wide and short, the root of the nose underdeveloped, the narrow palpebral slits emphasize by the epicanthus. These morphological characteristics are the most evident, but the condition is usually accompanied by a significant number of abnormalities, especially cardiac anomalies of varying degrees of severity, fissured tongue, abnormalities of the epidermal ridges and folds of the fingers (fingerprints) and of the palms of the

hands and feet. The main essential symptom of the syndrome is the mental deficit, which impacts with various seriousness but that rarely pushes the mental age of the person higher than that of a neurotypical child of 6–7 years old. In spite of all these difficulties, people with Down Syndrome can lead a fairly well-adapted life if the family environment is particularly favourable.

In 1866, the English physician John Langdon Haydon Down (Down, 1866) describes for the first time the set of traits commonly ascribed to the syndrome. However, it was not until 1959 in Paris that Jérôme Lejeune, Marthe Gautier and Raymond Turpin (Lejeune et al., 1959) demonstrated the cause of the syndrome: the Trisomy 21, a genetic mutation which results in the presence of three copies of the chromosome 21 (instead of the normal two) in the cells of people with Down's Syndrome. Simplifying (Le Méné, 2008, pp. 35–38), Lejeune, Gautier and Turpin hypothesized that this supernumerary chromosome is the result of an error in the distribution of chromosomes during the creation of reproductive cells. This discovery enriched the scientific knowledge on inheritance and opened a new field of research on human genetics, on the transmission of chromosomal aberrations. Indeed, up to that point Down syndrome was hypothesized to be linked to inheritance, but the laws of Mendel could not explain it. Trisomy 21 becomes the first example of a disease from chromosomal conditions in the human species, which is also the most frequent cause of the weakening of one of the most fundamental characteristics of mankind, intelligence. Not secondarily, with this scientific discovery Trisomy 21 was finally taken out of prejudice and the therapeutic dead-end to which it had been relegated: indeed, due to the approximative and culturally biased definition provided by Down ("Mongolian idiocy" or "Mongolism"), for over a century the syndrome had been considered to the likes of a negative racial trait, for which the affected people were left in the indifference of science due to their "regressive" status. This prejudice and suspicion of the public opinion was as strong also towards the parents of

the affected person, since it was supposed that their lifestyle brought the condition upon their descendants. The discovery of Lejeune and colleagues was the scientific breakthrough that the end of the XX Century needed, after the horrors of the concentration camps, the prejudice based on external traits and the segregation of the diverse.

The genomics laboratory presentation document (Laboratorio di Genomica–Università di Bologna, 2024) provides a quick summary of the laboratory research, which outlines the context for the present and potential future usage of the Machine. The line of research on Trisomy 21 started by Lejeune and colleagues was brought to Italy at the University of Bologna by Prof.ssa Maria Zannotti, who was a student of Prof. Lejeune in Paris in the '60s. The research is now carried on by the laboratory she contributed to create and which is now led by Prof. Pierluigi Strippoli. The research involves not only biochemical data analysis but also a fruitful collaboration between experimental and clinical researchers of the Unità Operativa di Neonatologia at the Policlinico Sant'Orsola-Malpighi in Bologna, which is aimed to improve the assistance of children with trisomy 21. The project *Genoma 21* is the largest clinical-experimental scientific research on Down's syndrome conducted in Italy and aimed at identifying a cure for the intellectual disability caused by the supernumerary chromosome 21.

The laboratory work currently focuses on two main subjects, which are strongly related to each other: the genetic study on the *critical region* of chromosome 21 and the metabolome (the set of metabolites) of trisomic cell models and of children with trisomy 21. The sample of children will also undergo thorough clinical and cognitive evaluation. This triangulation of complex and rich data should prove useful to identify specific altered metabolic reactions that could become effective therapeutic targets for the treatment of intellectual disability in Down syndrome.

Indeed, the intuition to study the relationship between mental deficiency and chromosomal diseases can be traced back

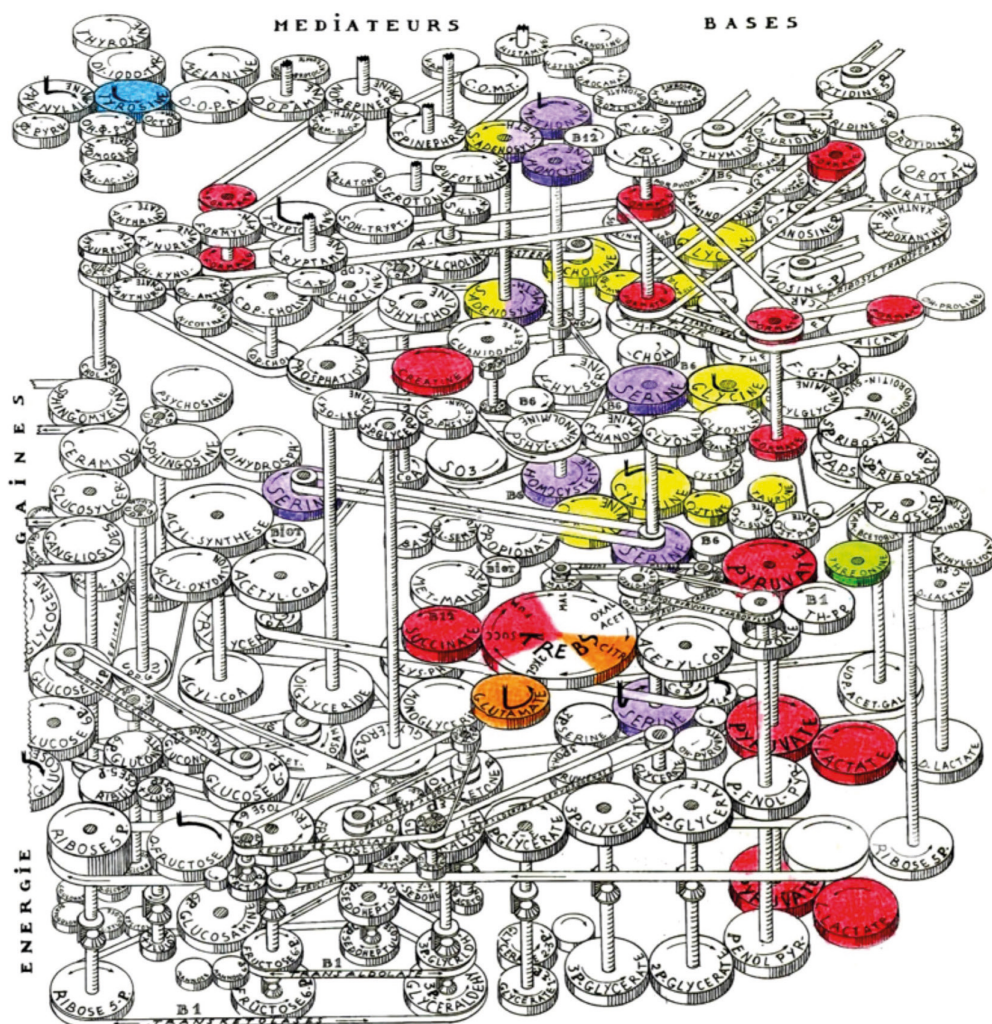
to Lejeune's articles (J. Lejeune, 1977), in which suggested practices to apply in concert: a pharmacological approach, general biochemistry and gene mapping to localize the main responsible genes of the disorders, all together.

In their quest to find Lejeune's theorized metabolic abnormality, by no coincidence the genomics laboratory research group took the Machine de Lejeune as a reference for mapping the metabolites in the plasma of children with trisomy 21 (Caracausi et al., 2018) (**Figure 3**). This scientific interest in the Machine deserves great attention from information designers because it is a sign of the heuristic value of the representation of the Machine. Indeed, according to Dr. Strippoli the Machine still incorporates a valid and useful model for their laboratory work.

Figure 3

The Machine de Lejeune, colourized by Caracausi et al. (2018).

Retrieved from Caracausi et al. (2018).



Note. The colour highlights altered concentration of metabolite concentrations: red = increased, with significance level and within expected range; orange = increased, but not at significance level and outside expected range; blue = decreased, with significance level and within expected range; green = decreased, but not at significance level and outside expected range; yellow/violet = increased/decreased, according to other literature data, respectively.

1.3.

Research questions articulation

In the previous section I mentioned how metaphors and analogies play a relevant role in the Machine de Lejeune, and that literature suggests that these cognitive devices can be helpful (or harmful) in the process of scientific discovery. This will also be discussed later in the dissertation.

However, the Machine is not a set of theoretical predicates, even though it informally incorporates some, and neither it is a sentence, even though it can be explained by means of some grammar. It is a visual communication artifact, whose author designed its *synsemia* (Perondi, 2012) to exploit a visual and conceptual analogy. Through the choices Lejeune made on the representation of the elements of knowledge in the biochemistry domain which he hypothesized to be relevant, Lejeune cast (quite figuratively) the shape of his own scientific model of cellular metabolism. Moreover, he purposefully chose a conceptual organization of the elements which shows heuristic value (see Chapter 2).

For this dissertation, the goal of the literature review and the analysis of the visual artifact from the information design standpoint is to derive a theoretical framework regarding concepts and constructs related to metaphor and analogy (as seen through the lens of different disciplines) that is relevant to the study of visual artifacts developed for scientific purposes, and which can provide a rationale to be reused to inform future information design works. To pursue this goal, the communication process between the author and the readers (mediated by the visual artifact) is investigated to describe how the information included in the model is made accessible to the readers, and which techniques the author employed in the effort towards minimizing ambiguity in the interpretation of the artifact. Chapter 5 synthesizes all the inputs.

Given this general direction, this dissertation tackles several problems:

1. To give a cohesive view of how metaphors and analogies are currently described as conceptual design devices in the design literature;
2. To provide an account of how analogy and metaphor are conceived by other disciplines and used for conceptual modelling;
3. To propose new practical ways to handle the inherent complexity of these rhetorical devices for the conscious design of visual artifacts.

While unfolding these topics, the research keeps the Machine de Lejeune as a reference artifact, allowing the reader to refer to a visual example of the proposed arguments.

The fundamental groundwork proposed in the dissertation can be taken a step further by adding more sophistication to the Machine model via mathematics and computing, as suggested in Chapter 6. Indeed, one of the objectives of this PhD project is to lay down the basis to produce in the future a computer model of the Machine, an interactive and visual access instrument to metabolism data, and to release it under a free software license to the biochemistry research community. The prospective effort is to allow in the future the research community in biochemistry to update and enrich the model with recent measurement data, making the Machine an actual instrument for studies on Trisomy 21 and for all other genetic conditions which impact on cellular metabolism.

Chapter after chapter, the reader will understand more in deep the Machine and how Lejeune conceived it as a communication artifact:

1. Which assumptions the representation is based on, how its components have been visually rendered;
2. How the readers of the Machine benefit from connecting two domains via analogy and how the analogue

representation supports in understanding the assumptions at the basis of the scientific model;

3. How the Machine expresses a heuristic value for the progress of biochemical research on Trisomy 21.

The basic assumption over the use of analogies and metaphors is that they should aid the conceptual modelling and the understanding of visual artifacts. The dissertation argues that if the analogy between two domains (biology and mechanics in the case of the Machine) is powerful, explicit and trustworthy enough to the readers, the rhetorical devices can gain some heuristic value or at least they can allow the readers to make inferences and hypotheses on relations between information in the source domain.

1.3.1. Sub-problems articulation

The fields of research involved in the study of a complex artifact such as the Machine are various. The topic is intrinsically trans-disciplinary, and even meta-disciplinary to some extent, embracing Information Design and Human-Computer Interaction, Philosophy of Science and representation of scientific models, and of course Biochemistry as the reference domain. Here follows the description of the sub-problems tackled in the dissertation to solve the primary research questions:

1. How literature in the design field proposes rhetorical devices such as analogy and metaphors as instruments for conceptual design;
2. Which concepts from the literature of other research fields can be integrated into the design one;
3. Problems with the definition or methodological use of these rhetorical devices in information design;
4. How metaphor and analogy relate to the definition of scientific models and to a visual representation such as the Machine;

5. What are historical examples of the usage of visual representations which convey models by means of a metaphor;
6. What are previous examples of biochemical representations and current standards, and how do they relate to a visual analogy such as the Machine;
7. Through which complementary communication the author strengthens the message conveyed by the visual representation to support the reader in appropriate understanding.

1.4.

Metabolomics and visualization. Comparisons with an analogue machinery

Before going more in-depth in the description of the visual analogy embedded in the Machine de Lejeune, we provide a quick overview of the research field that provides context to the artifact itself, which is the study of human metabolism, a specialized part of *metabolomics*.

Over the course of the XX century, the study of metabolism and its constituent chemical entities became more and more sophisticated, until at present times it is recognized as a specialized branch of biology defined as metabolomics. Idle & Gonzalez (2007) provide a useful introduction to the research field: metabolomics focuses on the systematic identification and quantitation of all metabolites in organisms (from bacteria to plants and mammals), with the aim to develop metabolic profiles of cells, tissues or organisms in relation to genetic variation or external stimuli. Contemporary technologies such as nuclear magnetic resonance, spectroscopy and mass spectrometry, and dedicated data analysis software provide enough resolution to simultaneously determine and compare thousands of chemical

entities within biological samples. In humans, metabolomics contributes to providing evidence on the ways our body metabolizes external chemicals, either by rendering them less or more toxic, or even carcinogenic, contributing to insights on the clinical use of drugs and drug development. Even in preclinical trials, after the administration of drugs the analysis of metabolites functions as fingerprints for organ-specific toxicities. A similar application of the study of changes in levels of metabolites is for tracing molecular biomarkers for gene deficiencies.

Popular contemporary visualizations of biochemistry and metabolomics, such as the KEGG Pathway diagrams (Kanehisa Laboratories, n.d.) (**Figure 4**, **Figure 5**), visualize the chain of metabolic reactions as flow diagrams. According to Dr. Strippoli, the most peculiar thing about Lejeune's choice of representation, as opposed to the more common flow diagrams, is to give a physically perceptible form to the Machine: Lejeune draws a "concrete" machine to analyze, understand, and fix, which stimulates the researcher to understand where this machine doesn't work as expected. Flowcharts (such as KEGG) can be strongly descriptive of the metabolic phenomenon, even at different levels of detail and for a variety of physiological or drug-related conditions. However, they generally fail to provide an overview that can be perceived as cohesive, and they somewhat force the reader to inspect each node of the diagram procedurally, while keeping in mind all the passages prior to and in between nodes.

In comparison to this choice of flow/network representations, the visual analogical format of the Machine makes a step towards closing the gap between the model and the audience, working on its communicative form. The representation conveys the idea of a mechanism that can jam or go out of phase, in which researchers can investigate and focus on finding its more critical areas. The accessibility of the information in the Machine is not solved by making the model simpler, as it is tougher to design a simpler representation than linked labels with implicit meaning as happens for the flow diagrams.

Figure 4
Regular map Notation, KEGG Pathway Map.
Kanehisa Laboratories. Retrieved July 02, 2021, from from https://www.genome.jp/kegg/document/help_pathway.html

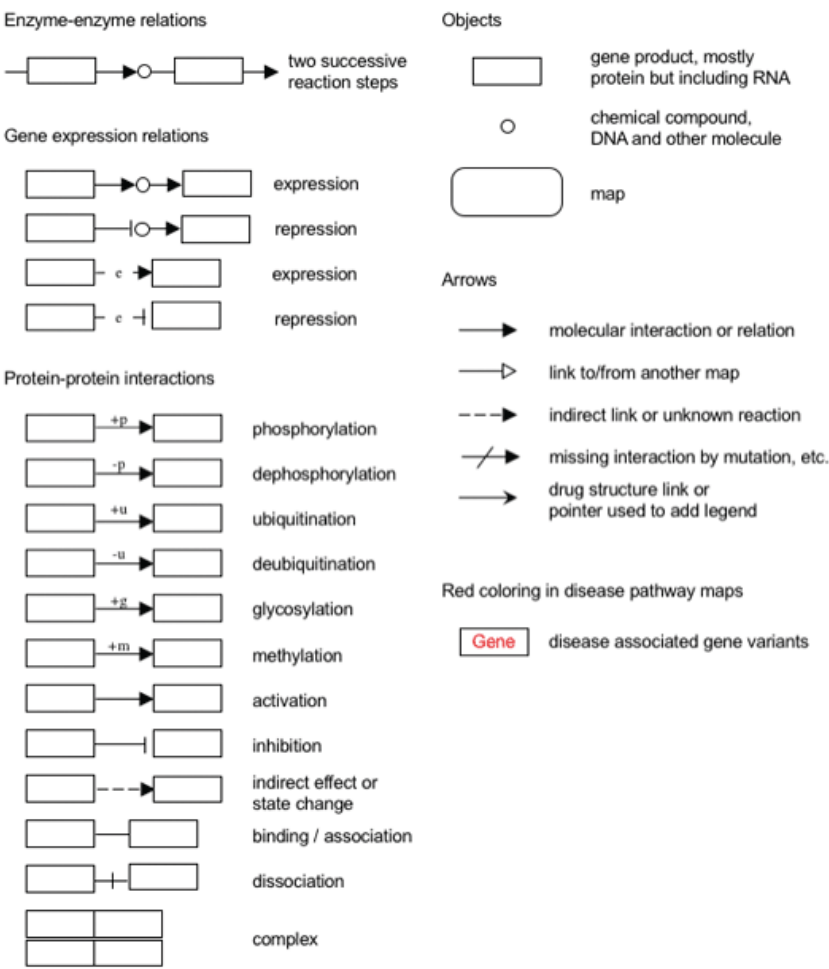
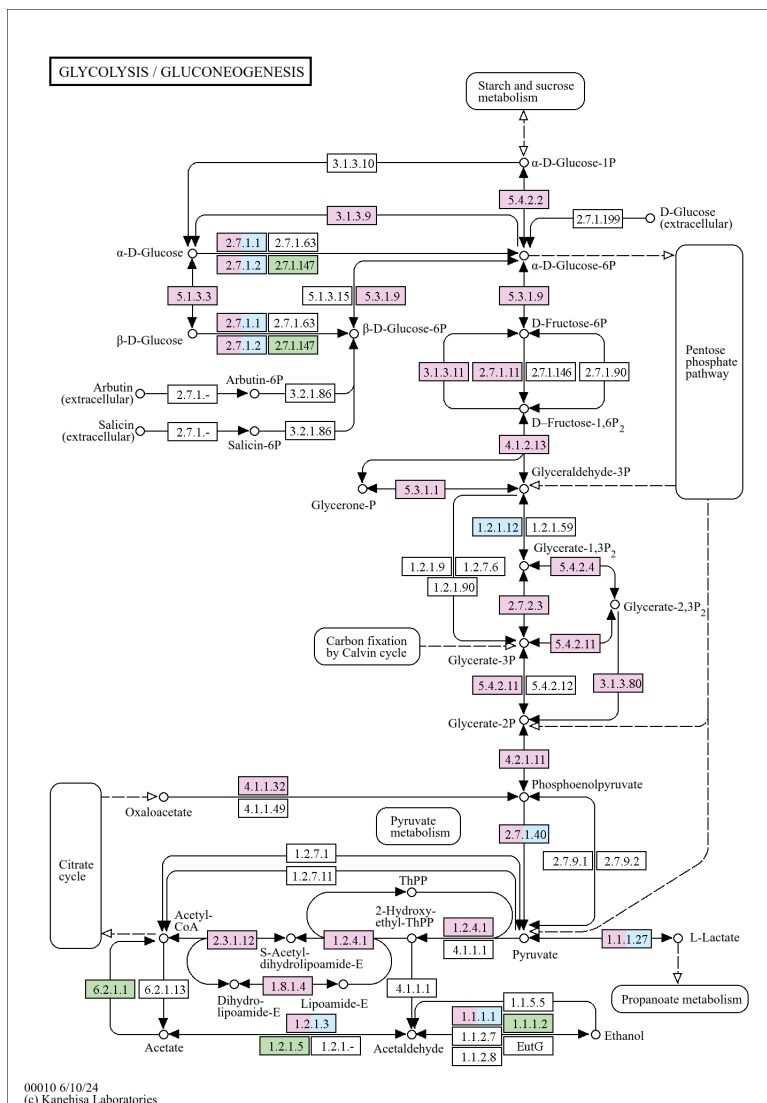


Figure 5

Example of a KEGG diagram of human metabolism. KEGG Pathway Map. Glycolysis / Gluconeogenesis - Homo sapiens (human) + Disease/drug. Kanehisa Laboratories. Retrieved July 02, 2021, from https://www.genome.jp/kegg-bin/show_pathway?map=hsadd00010



Quite the contrary, the same biochemical model is enriched with conceptual elements from another domain, mechanics, in an attempt to make the biochemical concept go through more effectively. While hoping to exploit this advantage in representation, the author accepts to face the risk of mismatching information and confusing further the reader, who is used to working mainly in the domain of biology and who is an expert in the representations for that specific domain. Lejeune faces this problem by providing detailed and easily accessible explanations of the analogical model, stating clearly its main value (heuristic) and limits (see Chapter 2.4). By doing so, he manufactures a powerful communication device, a one-of-a-kind, which can be considered both a scientific model worth mentioning and a remarkable example of communication design artifact stemming from deep knowledge and clear communicative intent.

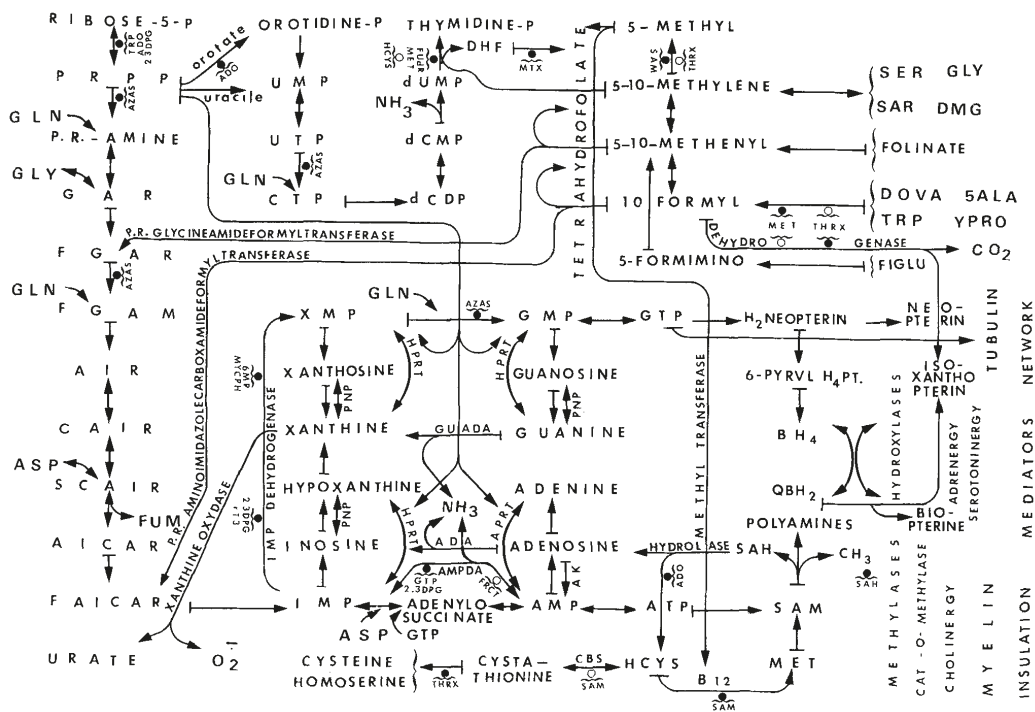
The creative ability to make up a completely new visual model did not prevent Lejeune from making ample use of flow/link diagrams to explain specific metabolic pathways and cycles, since this has been de facto a standard in the scientific communication in biochemistry that was already in use in the '70s (see Chapter 2.4.3, **Figure 14**). **Figure 6** is a practical example, in which Lejeune (J. Lejeune, 1990, 2005) illustrates the integrated functioning of the metabolic pathways involved in the monocarbons cycle (Chapter 2.4.3 will expand on this fundamental topic), to highlight how if the coordination of all the processes is disrupted by blockages in some stages it leads to collapse in the performance of the machinery, determining in turn mental retardation and even psychotic syndromes. Without going into detail on the scheme for the moment, it is worth noting the three labels on the right side of the diagram: *insulation*, *mediators* and *network*. These terms stem from the overarching analogy of the Machine (see Chapter 2.4.1), which Lejeune used for a long time to provide immediate context to his arguments. By reviewing Lejeune's scientific writing and talks (see Chapter 2), it emerges that he indeed relied more on the Machine as a model to express

his visions and hypotheses publicly than flow/link diagrams. The heuristic value of the Machine (see Chapters 2.1 and 2.4) served as a basis for general and detailed discourses on biochemical topics over the whole of Lejeune's career, permeating also less sophisticated forms of visual expression through simpler flow diagrams.

Figure 6

Example of a flow/link diagram on metabolism.

Diagram of the integrated functioning of the metabolic pathways around the monocarbons cycle. Retrieved from Lejeune (1990).



With the representation of the Machine, Jérôme Lejeune tries explicitly to cast an understandable form for a system of processes which are not directly observable, even though they can be measured empirically. The transformation of molecules (defined as *metabolites*, as part of the whole chain of reactions defined as *metabolism*), operated by and within human cells, can be acknowledged by the biochemical researcher through measurement of molecule concentrations in light of organic chemistry principles, not from direct visual inspection.

A peculiar feature of the Machine de Lejeune is that it is represented as an analogue computer, whose movement is deterministic: quantities (metabolites concentrations) are transformed on a continuum of values by conversion functions (chemical reactions). Lejeune himself (Lejeune, n.d.-c) describes the basis of this rationale: up until the early years of Lejeune's work, most of the genetic diseases had been explained in terms of mutation, a qualitative change in the DNA. If some portions of the chemical formula of the DNA are altered, abnormal amounts of proteins are produced, leading to specific biochemical alterations, which in turn determine the morphological or functional anomaly, that is the disease. However, in chromosomal aberrations, such as monosomies or trisomies, the hereditary message is not changed. The only anomaly is in the quantity, either omissions or repetitions of portions of DNA that are otherwise qualitatively normal.

FRA

Les récents développements de la cytogénétique humaine amènent à introduire un concept nouveau dans le déterminisme des maladies constitutionnelles, celui d'un effet quantitatif.

(Lejeune, 1966b)

ENG

Recent developments in human cytogenetics have led to the introduction of a new concept in the determinism of constitutional diseases, that of a quantitative effect.

Although the debate in biology is still open, for Dr. Strippoli (personal communication, December 23, 2019) the metabolism of a cell works similarly to such a deterministic mechanism: there has to be some regularity (and a form of determinism) in the functioning of the metabolism for it to function. If it would constantly change, there would be no life. At the molecular level, the single instance of interaction between metabolites and enzymes is difficult to classify rigidly, but by analyzing the whole set of reactions their interactions become statistically predictable.

Though, the determinism of the metabolism-mechanism does not imply conceptually an absolute rigidity of its inner workings, there is room for controlled variance: as Lejeune (1988) explains clearly, the cooperation of enzymes and compensation of the biochemical reactions is the fail-safe of nature. Some components double and take over others, to prevent catastrophic disasters, and these safety measures explain maybe why mental retardation exists at all. If no fallback systems were in place, every failure would lead to the complete neurological collapse, preventing survival altogether. But since there are fallback mechanisms, if one metabolic pathway is blocked it will result in some deleterious effects but it will be compensated sufficiently, avoiding complete breakdown.

Given all these premises, acknowledging the conceptual validity of the model and of the analogical representation of the Machine, a comparison with contemporary metabolomics visualization systems was performed to get a better understanding of what differentiates them from an analogical representation in the likes of the Machine.

Over the years, the research group at the Laboratory of Genomics studied and explored a variety of representation systems for the human metabolome. However, so far they have not really found a digital representation system which suits completely their investigations, both from a technical standpoint (database logic, input/output interface, data retrieval, etc)

and from a visual standpoint (organization of the information, relations between information, feedback on relevant features of the visualization, etc). This issue led the laboratory group to create their own custom tools, building databases from scratch but without a custom GUI. Interestingly, they had never really focused on elaborating further on the way the visual aspect of the output of their computations could better serve their research needs. On the other hand, they did acknowledge the uniqueness of the Machine the Lejeune as a conceptually and heuristically valid tool. We carried out a small literature review of metabolome information representation systems (Table 1), in order to assess their strength and weaknesses as representation systems for metabolomics investigations.

Table 1.

Reviewed resources on visualization of metabolomics.

Reference	Title	Topic
Angione, 2019	Human Systems Biology and Metabolic Modelling: A Review—From Disease Metabolism to Precision Medicine	Recent review which summarizes the last 15 years of metabolism modelling.
Aurich et al., 2016	MetaboTools: A Comprehensive Toolbox for Analysis of Genome-Scale Metabolic Models	Example of protocol for the development of a calculation programme which outputs a variety of plots to inform the biochemist.
Baart & Martens, 2012	Genome-Scale Metabolic Models: Reconstruction and Analysis.	Book chapter which discusses the operations behind the construction of datasets and models for metabolic investigations.
Chagoyen & Pazos, 2013	Tools for the functional interpretation of metabolomic experiments	List and comparison of metabolomic database web-based exploration tools up to 2013.

Reference	Title	Topic
Grace & Hudson, 2016	Processing and Visualization of Metabolomics Data Using R	Book chapter discussing a possible workflow for the computation of raw metabolomic data. It showcases several types of graphic outputs such as statistical plots, heat maps, box plots.
Gu et al., 2019	Current status and applications of genome-scale metabolic models	Genome-scale metabolic models (GEMs). The calculation they propose combines gene-protein-reaction. The paper also proposes a list of current software and databases with or without GUI for the exploration of metabolome data.
Henglin et al., 2019	A Single Visualization Technique for Displaying Multiple Metabolite-Phenotype Associations	“Rain plots”, which combine features of a rain-drop plot and heatmaps to convey the results of multiple association analyses. A rain plot can simultaneously indicate the effect size, directionality, and statistical significance of associations between metabolites and several traits.
Kanehisa Laboratories, n.d.	KEGG PATHWAY Database (https://www.genome.jp/kegg/pathway.html)	KEGG PATHWAY is an online collection of custom-drawn pathway maps, representing the knowledge of molecular interaction, reaction and relation networks. These are the classic maps of metabolism, static, which link metabolites to reactions.
Noronha et al., 2017	ReconMap: An interactive visualization of human metabolism	Web interface for the navigation, visualization of custom datasets, query and filtering of Recon 2, a genome-scale reconstruction of human metabolism.
Thiele et al., 2020	Personalized whole-body models integrate metabolism, physiology, and the gut microbiome	Models for human metabolism with several types of related graphic representations.
VMH (Virtual Metabolic Human) database, 2018	VMH (Virtual Metabolic Human) database (https://www.vmh.life/)	The VMH database is made of hundreds of manually curated genome-scale metabolic models, assembled based on genomic, biochemical, and physiological data. The online interface offers several types of graphic representations. However, it mostly shows classic metabolome maps linking metabolites by reactions, seemingly not in a quantitative way.
Xia Lab, McGill University, Montreal, 2021	MetaboAnalyst (v. 5.0) (https://www.metaboanalyst.ca/)	Web server for metabolomics data analysis, visualization and interpretation.

From this survey on the subject, the laboratory group's opinion is that no program seems to display metabolic data in a simple and intuitive way. These systems show weaknesses on the graphical side, and/or they are too complex to manage on a technical level (non-intuitive interfaces), and/or they lack the capacity to process data on the kinematics of biochemical reactions, especially when it comes to the opportunity to offer a dynamic simulation. Whether these software base their representations on numerical calculations on metabolism or they are simpler hand-drawn graphic representations of parts of the metabolism, they output static two-dimensional representations of the *links* between metabolites. The sheer density of information makes them tough to read, and unintuitive to navigate. Even if there is no motivation to doubt that the data behind the representation is accurate, their visualization says little to the biologist.

The uniqueness of the Machine as a representation in the scientific field is its ability to visually represent the analogy with an abstract physical engine. The shape of the Machine itself shows Lejeune's effort to make the relations between metabolites perceptible, more accessible and hopefully better comprehensible. Prof. Strippoli (personal communication, February 28, 2021) affirmed that "[the Machine ...] makes the links between the various elements almost 'physically' perceptible, in a three-dimensional way". This peculiar feature of the Machine, to be *perceptible* as a physical object even if it is an abstraction, a model, even a concept driven by ideology, can provide the researchers with inferences of a different quality than the other systems we reviewed.

How the representation of the Machine is able to *speak* to the biochemist in a more meaningful and even persuasive way is further detailed in the next chapter.

2.

Lejeune, scientific thinking

Lejeune's scientific articles, research notes, conference speeches, and divulgation talks are an invaluable source of information about the thought processes behind his scientific work on genomics and biochemistry, as much as about the Machine.

This chapter discusses materials from various sources, but a great part of the contributions were available for a period of time publicly in the archive section of the website of Fondation Jérôme Lejeune (Fondation Jérôme Lejeune, n.d.). The corpus included articles, book chapters and notes written by Lejeune over his whole career, counting an amount of 344 items. The documents are written in multiple languages, including French, English, Spanish, Danish, German, and Italian. Indeed, in his career, Lejeune travelled in several countries and had relations with scientific and political institutions, which required him to translate or produce documents in several languages.

For obvious research purposes, the group at the Laboratory of Genomics took great interest in the analysis of the corpus Lejeune's publications, to systematically inspect it for keywords depending on the specific research interest at hand, which could be a peculiar molecule, a determined enzyme or substrate and so on. On the design side, my interest was particularly towards the publications discussing the Machine, and I inspected the whole corpora for keywords like "machine", "analogy", "analogue", "analogie", "mechanism", "mécanisme", etc. This systematic search aimed to trace back the reasoning behind the Machine

and to detect when Lejeune discussed publicly about the Machine and the purpose this artifact served in his arguments. Moreover, the search made it possible to expand the focus from the Machine to the general way of reasoning of Lejeune, which the reader can appreciate how much it was tied to the use of metaphors and analogies to communicate what was known at the time, and what was still to be discovered.

Only a portion of the corpora is invested in the discussion of metabolism and what concerns the Machine. A great part of the publications from Lejeune is invested more in-depth into genome, genetic mechanisms, observation and clinical studies on people with monosomies and trisomies or other kinds of genetic conditions. Moreover, a good part of the documents, especially in the later stages of Lejeune's work and life, are devoted to discussions on ethics in medicine and biology. This dissertation will not cover these latter parts of the collected papers, due to the complexity of the topics, and also due to the unnecessary need to discuss ethical positions in this avenue. It is undoubtedly interesting, enriching and stimulating to discuss such important problems about life, freedom, self-determination, care, assistance and well-being, but they fall outside the scope of this dissertation. Such discussions deserve dedicated avenues for debate since these problems are not yet completely solved even in contemporary societies all across the world, and they are often still very much controversial despite being some of the most impactful on the lives of people. In any case, in the readings reported in this dissertation it is still possible to find some fundamental views of Lejeune on the world and medicine, since they permeated any discussion he made, obviously.

2.1.

A fundamental heuristic hypothesis

Lejeune (1966a, 1966b) provides a good introduction to the intuitions and findings of Lejeune in the field of cytogenetics and biochemistry at the time, which is fundamental to understanding both the context of research and the use of a visual artifact such as the Machine.

A basic concept in genetics is that one gene controls one enzyme or one specific protein, therefore it controls more or less directly the manifestation of specific traits. A given segment of the genome can produce a specific clinical entity that is recognizable. The relationship between problems with enzymes though does not correlate directly with that structural gene of that enzyme, but it is a good hint that the thing controlling the problem is located on that chromosome.

As already mentioned in Chapter 1.2, Lejeune and colleagues demonstrated in 1959 that supernumerary chromosomes in the human genome, like in Trisomy 21, create determined clinical conditions. In 1963 (Le Méné, 2008, pp. 35–36) Lejeune and colleagues also demonstrated that the lack of one element of the genome (the monosomy, the opposite of the trisomy) determines in the human species clinically recognizable diseases, one of the most know is the “Cri-du-Chat” (the disease of the “Cat mew”, since amongst the symptoms the most striking one is the tonality emitted by the person, similar to the mew of a cat). This further evidence leads Lejeune to classify chromosomal conditions in several ways, but first as the opposition between excess or defect of chromosomes.

Given the possibility to detect chromosomal aberrations—therefore monosomies and trisomies, as opposed to the normal expression of couples of genes—and the consequent opportunity to link the excess or the defect of a given chromosome to the variation of the phenotype (i.e the physiology, the behaviour,

etc), a simple hypothesis or logical model with heuristic nature can be made to direct future enquiries (Lejeune, 1966b): since genes control the production of enzymes, an excess of a given gene should result in an excess of the corresponding enzyme as follows:

- monosomy: 1 gene produces in the cells 1 unit of enzyme activity
- normal: 2 genes produce in the cells 2 units of enzyme activity
- trisomy: 3 genes produce in the cells 3 units of enzyme activity

Consequently, compared to normal conditions with two genes, the change of ratios will be in different directions in monosomy and in trisomy: comparing normal subjects with trisomic subjects, the ratio of comparison of the enzymes is 2:3, or a factor of 1.5; comparing monosomic and trisomic subjects, the expected ratio should be 1:3, or a factor of 3. Even though this rationale is most likely an oversimplification, it provides enough hints to check whether for simple biochemical characteristics the monosomy should determine a decrease and trisomy an increase in the enzymatic reactions directly controlled by the genes in question. Lejeune (n.d.-a, n.d.-b, 1982) brings up evidence in literature of such variances of 1.5 times in enzymatic activity for superoxide dismutase (SOD I) in Trisomy 21 (since the enzyme is controlled by the genes located in chromosome 21) and for lactate dehydrogenase-B (LDH-B) in Trisomy 12p.

Even if Lejeune (n.d.-a, 1966a, 1966b) recognized how simple (*naive*, sic.) this basic arithmetic relation of unit of gene to unit of enzyme, the experiments seem to warrant this hypothesis, which heuristic value then leads to suppose that in the case of excess of enzymes the chemical reactions are going *too fast*, while if there is not enough enzyme they are going *too slowly*, even though in both cases the quality of the reaction is normal. The two conditions, trisomy and monosomy (defined by Lejeune as “countertypes”) should then look like mirror images diverging

from a normal condition, and for a variety of symptoms they appear to be.

One gene—one enzyme, three genes—three enzymes is extremely naive indeed. Nevertheless, even if not exactly true, this model does have a great heuristic interest. If it represents a part of the truth, it would mean that in chromosomal imbalance, children have the whole biochemical machinery right at hand with just some steps running too fast or too slow. (Lejeune, 1966a)

However, the heuristic seems to work mostly for minor symptoms, while the two conditions are alike for the major symptoms, they share traits like mental retardation. The analogy in Chapter 2.3.2 helps to clarify the topic.

Summarizing from Lejeune (1964), beyond the analysis of the chromosomes and their aberrations like in trisomies, which was well established by Lejeune and colleagues, the subsequent line of work which was followed by Lejeune and the cytogenetics research community tended to detect which biochemical mechanisms are accelerated or slowed down by a given chromosomal anomaly. The aim, in the case of Trisomy 21 for example, is to define precisely which biochemical reactions are controlled by chromosome 21, and accelerated by the presence of three chromosomes 21 (instead of the normal two), so that to counteract them by suppressing the activity of these excess reactions to bring them back to a normal balance. The analogy in Chapter 2.3.1 helps to understand the issue better. The “therapeutic arsenal” (Lejeune, 1972) with which counteract the adverse effects of the genetic conditions on the biochemical side could be, at the time, supplying the missing enzyme (like insulin in diabetes), to administer drugs by supplying antimetabolites of accelerated biochemical reactions (e.g. antithyroid drugs), reducing the intake of precursors of the toxic agents through a dedicated diet, and so on.

FRA

Il est fort important de savoir en effet que les trisomiques possèdent toute la machinerie génétique, sans aucune erreur dans les plans de construction et qu'ils souffrent seulement d'un excès d'information

(Lejeune, 1966b)

ENG

It is very important to know that people with trisomy possess the entire genetic machinery, without any errors in the construction plans, and that they only suffer from an excess of information

Lejeune, as early as in the '60s (Lejeune, 1966b), advocates that these theoretical considerations were still based on very fragmentary data, but that it was worthwhile building a *logical model* right away, to compare it with experience later. Diagramming and scheming possible theories was a way to show that reasoning can lead to a search for the existence of precise biochemical mechanisms and to guide the search according to a heuristic approach (Lejeune, 1972a). In this context, Lejeune defines the heuristic aim of the logical model as a means to direct research towards experiments capable of providing the elements for a detailed answer (Lejeune, 1979).

This core idea leads later on to the definition of a very basic logical model based on simple quantities and ratios such as the Machine (see Chapter 2.4). The urgent need Lejeune felt to treat patients (Lejeune, 1972b), to alleviate their condition, made him decide to start even with this invented model of machines that simulate some effects of intelligence. Urgency he justified by the necessary long time required by neurology and neurophysiology to clarify sufficiently on the relationships between the nervous system and the functions of the mind. This does not mean that the biological and psychological models cannot coexist (Le Méné, 2008, p. 107), quite the contrary: biochemistry investigation is not "more scientific", it is just more simple, as it allows to isolate factors that are timeless within the organism, while psychology has a more complex task to investigate the nature of individuals, which varies in time and from person to person.

Both approaches are valid and should be persevered together focusing on the person as a whole. Given the urgency, Lejeune focuses his efforts on where optimistically there are fewer resistances to find effective solutions. Therapies for treating the symptoms were already present, as mentioned above, but the specific target for those treatments was to be better understood in order to make the treatments more efficient.

FRA

[...] le vrai retard de la médecine de l'intelligence n'est pas dans la thérapeutique mais bien dans la compréhension de la maladie elle-même. D'où la nécessité de l'approche heuristique que nous venons de proposer.

(Lejeune, 1972b)

ENG

[...] the real delay of the medicine of intelligence lies not in therapies but in understanding the disease itself. Hence the need for the heuristic approach we have just proposed.

Given the primary focus on the nervous system and cognitive functions, the Machine in its most complete form (Figure 1, see Chapter 1.1) does not portray the complete set of metabolites for all the biological functions of the human body, but it comes *pre-filtered* on the main chemical mechanisms and enzymatic reactions essential to the functioning of nervous cells (Lejeune, n.d.-b, 1979, 1981b). Focus is a prerequisite for the heuristic approach, as it is described in Chapters 2.4.2 and 2.4.3.

Following on this pragmatic view of Lejeune for his model, it is also important to remember that the representation of the Machine is described by Lejeune as being a “pseudo-pascalian” machine because it does not include all the components of the Pascal calculator. Indeed only the internal gears of the machine are represented, the actual (and conceptual) calculating mechanism. This oversimplification is instrumental to both simplifying the message (embedded visual representation) at its core and also to expose the heuristic value of the visual model. As Lejeune describes (Le Méné, 2008, p. 106), the best way in biochemistry

to find the root causes of imbalances and diseases is to look at the gears of the Pascaline, searching for the gear which represents the units. When this gear completes a full round, it will trigger the gear of the tens, and so on. Needless to say, the complex mechanism does not have to be rendered in all its detail to achieve this communication effect (implying that the communication partner should understand this basic concept about the Pascalian calculator from the beginning).

The following chapters will better explain Lejeune's visions on cytogenetics, the work to be done in biochemistry and the overall objectives of his lifelong scientific endeavours.

2.2.

The disinherited children

After having explained the basic components of the genetics and biochemistry domains Lejeune worked on, before going down to details towards which parts of such work became relevant for the Machine, another fundamental introduction to Lejeune's deepest convictions is due. Powerful visions, and faith, towards a positive future moved the work of the scientist, influencing deeply his reasonings in the domain of biochemistry and genetics. These visions led him to conceive the problem of disability as something to tackle as a whole, investigating not only the inherent biochemical mechanisms but also looking directly at the people affected and their families. This chapter contributes to providing a key for the interpretation of Lejeune's writings, as much as to better understand the role which the Machine played and can still play in those research fields. Put simply, visions lead actions and give shape to the studies and artifacts that people produce to achieve their goals. Elucidating the visions seems a good starting point.

The research efforts of Lejeune and his colleagues are directed towards those people whom he (Lejeune, n.d.-c, 1966a) describes as the *disinherited children*: since they have not received an equitable genetic patrimony, they are in the true sense of the term the most disinherited of the children. While acknowledging how uncertain the heuristic hypotheses on gene dosage and metabolism are, Lejeune (Lejeune, n.d.-c, 1964) is determined to follow them in the hope of providing a different future for these disinherited children, who seem to be otherwise condemned to a life with no options.

FRA

Pour incertaines qu'elles soient, ces hypothèses ont l'avantage d'orienter la recherche vers une tâche qui, si elle aboutit, sera la plus gratifiante possible; le premier espoir raisonnable de changer enfin le destin de ces enfants déshérités qu'une erreur de mécanique chromosomique condamne inexorablement à l'imbécillité et à la difformité

(Lejeune, 1964)

ENG

However uncertain these hypotheses may be, they do have the advantage of directing research towards a task which, if it succeeds, will be as rewarding as possible; the first reasonable hope of finally changing the destiny of these disinherited children who are inexorably condemned to imbecility and deformity by a chromosomal mechanical error

Reflecting on numbers, Lejeune (Lejeune, n.d.-c, 1966a) highlights that if we consider that a chromosomal anomaly severely affects one child in a hundred at birth, the issue of finding metabolic treatments is ever-pressing. These people will otherwise suffer physical and mental issues for all their lives. Collecting knowledge of the metabolic disorders caused by chromosomal anomalies would make it possible to use antimetabolites to slow down the accelerated reactions or to compensate for the deficient metabolism.

For Lejeune (1970), the efforts of the scientific enquiries towards finding a metabolic cure to the issues caused by genetic conditions are strongly rooted in the ethical and also

very practical stance to face the medical condition, rather than preventing the children with disability from being born. This moral imperative permeates all his work, and it is inevitably inherent in his publications as much as in his private life.

we human geneticists have to face everyday reality: disabled children and distressed parents exist (Lejeune, 1970)

In his view (Lejeune, 1972b), medicine in this field has no presumption in attempting to cure mental deficiencies and it will not claim to restore the mind to those people who will always be affected by a deficiency. The aim of medicine is to provide those people with the means to make the best use of their own intelligence by compensating for the failings of an imperfect biological network.

Lejeunes' career develops in decades in which the ethical and political debate around prenatal testing and abortion are as controversial as ever. In 1972 in France (C. Lejeune, 2008, pp. 51–52), the legislative proposal by Dr. Peyret reignited the debate on abortion, which since 1920 had been totally illegal in the state. Eminent scientists, including Lejeune, took part publicly in the scientific debate. His position is against abortion (Lejeune, 2002, pp. 60–67, 192), pushing for the search for metabolic cures *in utero* instead, had him criticized quite loudly during his whole career, beyond his scientific arguments.

Lejeune (1980) acknowledges how in those early decades of cytogenetics the progress of genetic technology has directed its efforts divergently with respect to his own vision of cure: some biochemical errors and significant chromosomal defects can be detected early, *in utero*, by analyzing the fetal cells floating in the amniotic fluid. The tendency of medicine has become therefore to propose systematic screening and the selective abortion of the fetuses as a way to manage the genetic disease. This leads to ethical dilemmas (especially for the parents) in deciding whether to keep or not the babies. The tendency to practice

“selective destruction” is what Lejeune describes as a sort of sophisticated racism based on molecular or chromosomal discrimination. For him, medicine can provide a third way.

Suppression or repression of unfit or unconformed ameliorates the statistics but not the heart of societies. Only an intimate union of heart and of reason will salvage someday human intelligence (Lejeune, 1980)

A remarkable trait of Lejeune’s personality is that, even though he was a man of great Catholic faith, his ethical positions were not based on religion, but rather on his principles of doctor and his scientific knowledge (C. Lejeune, 2008, pp. 109–110; Le Méné, 2008, p. 48): every human being has the right to life and dignity and, if they are ill, to the support from the whole society, not to death. Lejeune (1970) advocates that the work of geneticists should be guided by two sentiments: humility, since genetics have not ready-made answers to offer and the secret of the human condition has not been broken yet; compassion, since even the most disinherited (disabled) people belong to mankind, and because the sorrow of the parents cannot be consoled by science. For him, medicine should not propose to eliminate the people who cannot be helped yet, but to strive to fight for life and health and against disease and death. Even if it happens that nature condemns—sometimes the anomaly is too much for nature to carry on—the duty of medicine and genetics is to not inflict the sentence but to try to commute the pain. For him (Le Méné, 2008, p. 21) the vision of the observer (the doctor, the specialist) cannot be neutral, in the same way test results or therapeutic conclusions are not. Indeed, the same people who can decide to eliminate a problem can also find a way to cure it.

During an ONU assembly on abortion (C. Lejeune, 2008, p. 53), this vision led him to define the institutions allowing abortion as “institutions of death” instead of “institutions of health”. After the speech, he was convinced that by expressing those

opinions he had precluded himself from winning the Nobel Prize. Which he was never awarded, for this or other reasons. Regardless of the sensitivity each one possesses, of the position taken to being pro- or against prenatal testing and abortion, these were the strong beliefs and vision driving the work of a man who devoted his life to finding cures for people with severe genetic conditions.

What Lejeune (1972a) remarks is that the greatest difficulty in conducting such research, which unfortunately discourages a large number of laboratories, is that mental retardation is an illness for the patient and his family, but it is only a symptom for the biologist. Human genetics shows that a multitude of errors, from chromosomal aberrations to the most localized chemical disorders, can lead to the same consequence, the “amputation” of the mind (“l’amputation de l’esprit”, sic.). Acknowledging such a terrible catalogue of conditions, the great temptation is to give up looking for a logical model that can enable researchers to order this jumble. Yet, it is possible to conceive a model, even a tentative one: a machine to simulate certain effects of intelligence, the computer, in its abstract conception of information flow into matter which has properties, limits, and failures. The most basic form of computer, the Pascalian calculator, can showcase these features in the simplest form.

2.3.

Metaphors and analogies in Lejeune’s scientific writings

Based on publications, the Machine drawing dates around 1976–1978. However, such complex visualization could not have come out of thin air: several of Lejeune’s reflections on the domain of mechanics predate the Machine by about twenty years. More than this, Lejeune’s writings showcase how habitual

it was for the scientist to make significant use of metaphors and analogies, with different domains, to help himself in expressing intuitions on complex and invisible phenomena. Intuitions which ultimately led his work and views on the world until the very end. Indeed, it is possible to notice how the timespan within which Lejeune uses these rhetorical devices covers pretty much the lifetime of his work. The basis of the intuition of Lejeune remained pretty much the same over the years, and curiously the examples he made remained fundamentally similar, even if after some decades he updated a bit the vocabulary and the details included in the narration.

Not surprisingly, these narrations from Lejeune support the audience in getting acquainted with the topic of the study of the biochemistry of metabolism, its relation with the human genome, and overall the line of study followed (and partially started anew) by Lejeune and colleagues. The use of metaphors and analogies makes the complexity of this research field available to non-specialized audiences, designers included of course.

It is clear that Lejeune was passionate about mechanics and cars. The preface to his daughter's memories book (Casini, 2008a, p. 12) describes how the man was always eager to "speak in parables" to make complex scientific reasoning more understandable to the listener, and how skilled he was at manual repairs. These predispositions and passions permeated his work and his way of conceiving intellectual challenges.

The following chapters propose a series of fruitful and significant analogies and metaphors proposed by Lejeune, found amongst his publications.

2.3.1. Genes and chromosomes - The fifth spark plug

Lejeune (n.d.-c, 1964) describes how at the origin of mental retardation there can be chromosomal aberrations. Human genes, to be found on chromosomes, determine the production

of enzymes which, in turn, control the biochemical reactions by which the cells live and multiply. The fundamental reason for the harmful effect of an excess of chromosomes and their genes, as it happens in Trisomy 21 for example, is the excess of activity of the enzymes that are controlled by those genes, which disrupts the overall cell metabolism.

To express this concept, Lejeune (1964) makes an analogy with car mechanics, to explain his vision of how Trisomies affect human metabolism and ultimately have repercussions on subjects' intelligence and quality of life.

To make an analogy, Lejeune proposes the example of a 4-cylinder car engine: adding a fifth spark plug, even if it is completely normal and works perfectly, will not improve the engine at all. Quite the opposite, there would be a chance that the explosions which the additional plug induces will occur at the wrong time, hampering the rhythm of the engine and therefore reducing the efficiency of the machine. Disconnecting the supernumerary candle that causes the explosions at the wrong time would bring the engine back to its normal and efficient working. In biology terms, this means detecting and partially blocking the activity of the chemical reactions involved in the imbalance, bringing them back to a normal balance. This analogy dating around 1964 plays a fundamental role in Lejeune's subsequent work on cytogenetics and biochemistry. It creates the premises of a heuristic use of the model for the Machine, discussed in Chapter 2.4.

Lejeune (1988) acknowledges that a good car repairman would delicately disconnect the extra spark plug and therefore fix the engine back to normal conditions. But with the genetics knowledge at the time, there was no way to unplug the extra chromosome altogether (neither there is yet), even if the progress in the field is constant. Until when this will be possible, the focus can be on understanding why and how the excess of the genes impairs the functioning of nerve cells, preventing the full development of intellect. So instead of "unplugging the

spark plugs”, the effort focuses on the regulation of the “carburation” of the engine.

FRA

Ici aussi une image grossière empruntée
à la mécanique nous permettra d’abrégier
une difficile discussion

(Lejeune, 1964)

ENG

Here again, a crude image borrowed from
mechanics will enable us to shorten a
difficult discussion

Extending on this concept of the engine (Lejeune, n.d.-c, 1964), focusing on the whole vehicle (the human in its completeness), Lejeune proposes another analogy: if a car is correctly built and driven, it should reach its top speed as defined by its construction. By studying the functioning of a complex machine, like a car, we can measure its highest function, that is its top speed. This top speed is going to be probably the first feature to suffer anomalies from any modification made to the prototype, whether the windows are open, the tyres are insufficiently inflated, the bodywork is deformed, the fuel is of inferior quality, or the driver’s position is altered. Human intelligence can be considered the “top speed” of living matter; any disruption to the cells’ inner mechanisms almost always has repercussions. As a general consideration, in an extremely complex and highly integrated system, any change is likely to produce, besides its specific aspects, some degradation of the best performance of the system. Of all the organism’s functions, intelligence is the one most strongly affected by excess of autosomal material (chromosomes), leading subjects to have mental retardation as a common consequence. Indeed, in very different conditions stemming from anomalies on chromosomes 21, 13 and 18, especially in the most serious cases, the most dramatic deficit is in intelligence.

2.3.2. Imbalance from opposite causes - The orchestra cacophony

Lejeune (1966b) illustrates how the simple heuristic rationale of the ratio of comparison of the enzymes seems to be reflected by minor morphological characteristics, as variations from the normal condition and as reciprocal between monosomy and trisomy. On the other hand, complex symptoms such as mental retardation and developmental delay are often shared between both conditions, and it is difficult to relate the expected enzyme/gene dosage to this high-level function since it results from both defect and excess. Moreover, sometimes when both conditions are extremely severe, the abnormality of the chromosomal material brings both conditions to the same consequence, to stop the mechanism, hence death.

To explain this phenomenon of similarity of effects resulting from opposite causes, Lejeune (1966b) proposes an analogy with an orchestra in which musicians decide to play their score at a different speed from that of the ensemble: the result is always cacophony, it doesn't matter whether their tempo is faster or slower. In biology terms, the cacophony is pretty much the phenotypic manifestation of the condition.

However, if we can single out the two conditions, one going faster than normal, and the other going slower, then it is like witnessing the musician changing his tempo not during a *tutti* but during a *solo*: changing *moderato* to *prestissimo* will produce one symptom and the change to a *largo* will make the contrary. These variations make it possible to recognize the *countertypes*, mirroring each other.

This change of "tempo" in biology is to be considered normal for morphological traits, within some degree of liberty in their expression, and it leads to the differences found in normal subjects. It becomes abnormal due to genetic conditions.

2.3.3. The emergence of species - The automotive factory

The following metaphor has been proposed by Lejeune in one of the many public debates about high-level topics in science, ethics and politics (Lejeune, 1993). Lejeune has been an important voice in the international debate throughout his whole life and career, leading him also to become a member of the Pontificia Accademia delle Scienze in 1974 and then president of the Pontificia Accademia per la Vita in 1994 for a short while, before passing away the same year.

Without going too much down into the debate, and regardless of the ethical and political position the reader takes, the metaphor enlightens how Lejeune makes use of his fluency with the automotive world to convey his vision of human life. The reader can also appreciate the funniness of the metaphor, which contributes to the memorability of the discussion.

FRA	ENG
Chaque mécanisme de la vie telle que nous la connaissons trouve un équivalent ou une analogie dans les mécanismes complexes d’une usine moderne.	Every mechanism of life as we know it finds an equivalent or analogy in the complex mechanisms of a modern factory.

(Lejeune, 1993)

A automotive modern factory, highly robotised, can be seen as a reproductive apparatus. Every car (every specimen of the “species”) exiting the assembly line strictly follows the instructions contained in the memories of the factory computers, which are stored and locked away safely, like the DNA wound up in chromosomes is locked away in the nucleus of reproductive cells.

The remarkable phenomenon of cerebration (the increase of brain mass and functions) in living beings can be conceived as the proliferation in recent years of computerized systems into the mechanics of the car, which implies an explosion in the coordination between computers and mechanics.

The progression of morphological traits in the lineages of living beings over generations can be exemplified by the stages in the evolution of luminous apparatus in cars: in the oldest fossil, the horse-drawn carriage, lanterns were hung on the sides of the passenger compartment. Slowly, the lanterns moved forward, to the sides of the engine and eventually on the front of the radiator, converting also into light bulbs. The first displacement of the lights was raised at the top of the radiator, like the eyes of molluscs. Then, the environmental pressure (the laws of aerodynamics) made emerge three mutant competitors: lights enclosed in the radiator grid (like the old Peugeot), or recessed into the front wings (like the old Renaults or Panhards), or wedged between the engine and the wings (like the Opels or the Renault Juvaquatre). Different models provide examples of developments which eventually converged. Like in living beings, development to higher forms led the initial external setup of the eyes recess into the cranial cavity: the “auto sapiens” is the appearance now fixed for the time being.

The success of a car model is determined by the market, by the choice of the consumer towards its various characteristics, either regarding the appearance of the bodywork (the phenotypic selection) or the performance and economy (the physiology). The amount of units produced and sold seems to determine the success in the competition between brands, leading them to expand or close factories. This could lead us to think that the most numerous offspring (model) determines the winner in the “natural selection”. However, while we know much about how cars are produced, there are no cases of self-reproduction in cars. This is where the natural phenomenon of reproduction escapes the simple logic of numbers. Nature does not throw away species (shutting down facilities for those models) if they do not perform the best in every sense, and there are no models which are completely new. It would be too much of a waste of progressive changes that are calculated, not due by chance. To synthesize (Le Méné, 2008, pp. 78–83; Lejeune, 1993; Lejeune,

2002, pp. 85–87), indeed such evolutionary theory can explain only variations within the same species, since the adaptation to local unfavourable conditions cannot be considered a progress of species. Genetics and the study of karyotype provide a much more sophisticated picture of the discoveries of the past and the projection to the future of the study of life. Nature requires organisms to make “jumps” to create new species, a phenomenon that otherwise cannot be explained through the progressive evolution of traits. Individuals with coherent genetic mutations within a species make fertile offsprings with a new, recombined set of chromosomes, which cannot recombine their genes anymore with their ancestors. A new species is then defined, and it has the potential to proliferate.

We will not go further in the discourse, since it embraces many topics that fall beyond the limits of this dissertation. The article from Lejeune (1993) is of great interest though, it is worth reading it fully. What is worth noticing is how Lejeune showcases all his interest towards cars and mechanics, bringing him to form a narrative metaphor to explain his view on evolution and genetics. The vision of Lejeune on the human body is holistically related to the concept of complex machines and engines. The Machine is part of this vision of life and complexity.

The arguments Lejeune brings up suggest that good science, good practice, good mindset, come out of interest in various and apparently unrelated domains. Analogies and metaphors are such powerful rhetorical and thinking devices, and they rely on the fact that the thinker is able to make meaningful connections between domains. Everybody, and especially designers, can make use of these thinking devices only if they are deeply interested in different domains. This is not a generic statement, of course the more a person has varied interests the richer can be his/her view of the world, but also the more detailed and fruitful analogies and metaphors can become.

2.4.

The Machine in Lejeune's scientific writings

As already shown in Chapter 2.3.1 and also from what the following chapter illustrates, it becomes evident that the origin of Lejeune's intuition to make a fruitful analogy between the domains of biochemistry and mechanics can be traced back a few years before he showcased the drawn model of the Machine. Indeed, these reflections are fundamental and generative to the way such visual representation could be laid out, and to the way the contents (the elements of knowledge) were selected and related to each other. Lejeune was knowledgeable and passionate about mechanics and electronics, cars and computers included. From such a predisposition, significant relations between domains were born.

From Lejeune's publications and discourses, it is possible to trace macro and micro aspects of the analogy. These different levels of complexity are each related to characteristics of the design of the Machine visual representation, and they help understand better which conceptual tools the designer can use to support the development of a fruitful visual analogy. The subsequent chapters are dedicated to better explaining these tools, starting from the very practical example of the Machine.

2.4.1. Intelligence and the machine

The title of this chapter is borrowed from the title of a chapter by Lejeune (1972b), "*L'intelligence et la machine*", and for a good reason: as described below, Lejeune relies heavily on the analogy between human intelligence as a result of a perfect and delicate balance of the organism, and the high performance of a computer or a machine whenever all its components are working *as intended*. He explicits what are the objectives of using a

heuristic approach to investigate the metabolism of people with genetic conditions as if it were a machine to analyze, section, test and one day also empirically observe. These objectives are inherently linked to the choice of a representation of a machine, as much as they define what are the high-level positive traits (see Chapter 4.3.2 of the analogy between the representation of a pseudo-pascalian machine with the concept of metabolism.

Lejeune (n.d.-b, 1972a, 1972b, 1981a, 1982, 1984, 1990, 1992) provides accounts of the vision of the Machine, opening to the hypothesis to create a heuristic model for the investigation of metabolites. Looking at the general context, he prefaces that by no means taking the *computer* as a model implies that the medium of human intelligence is built similarly—since the building materials of machines have little to no relation to the biochemical functioning of the brain—or that intelligence even performs according to the same laws of a machine, since the complexity of the network of neurons in the human brain is on a different order of magnitude in comparison to any machine.

Machines make use of a broad range of physical phenomena to work too, from the geometric invariance of solid matter shaped into wheels and linkages of a pseudo-pascalian machine, to the directed flow of electrons of advanced computers, semiconductors, fluid dynamics and electromagnetism. Even so, the conditions recognised as necessary for a machine to function properly seem to all satisfy apparently imperative requirements, or operating conditions:

1. A **network**, a complex multitude of circuits which potentially have a logical meaning, that is rigorously established and which determines a precise series of cascading effects;
2. **Components** with a punctual and closely defined action, always the same and always triggered under identical conditions, capable of combining volleys of impulses. Each component obeys strictly to its own laws of action;
3. A multitude of **connections**, which are oriented to transmit the effects of one component to others and to carefully

avoid any parasitic diffusion. The circuits have switches which define the path of information, and all the remote links are correctly isolated from each other.

- 4. The **speed** of the elementary process cannot be altered, it is of absolute importance that the chain of effects takes place over a specific period, allowing the consequences of a circuit to be compared with the results by another circuit.

What Lejeune highlights is that these characteristics could be necessary for intelligence to develop, and which genetic conditions might hinder it. This can be considered the core of the concept of the Machine. The brain is conceived (Lejeune, 1990, 1992) as an incredibly fast counter of particles, capable of bringing order to entropy, rejecting the fortuitous and retaining only the deducible, the essence of reason.

FRA	ENG
Il est dès lors possible que les conditions reconnues nécessaires au bon fonctionnement d’une machine soient nécessaires aussi à l’épanouissement de l’intelligence, à côté de beaucoup d’autres que nous ignorons entièrement. Il se pourrait ainsi que les “pannes” susceptibles de gêner le fonctionnement des machines puissent nous indiquer par simple analogie le point d’impact des conditions génétiques qui font d’un malade un débile mental.	It is therefore possible that the conditions recognised as necessary for the correct working of a machine are also necessary for intelligence to develop and flourish, alongside many others that we ignore completely. It could be that the “faults” which hinder the functioning of machines can indicate to us by simple analogy the point of impact of the genetic conditions which make a patient mentally disabled.

(Lejeune, 1972a)

Even if this vision necessarily oversimplifies biology, Lejeune (Lejeune, n.d.-a, 1972a, 1972b, 1981a, 1982, 1984; Le Méné, 2008, pp. 91–108) uses it to express failures in the machine located in each of the three (plus a consequential one) fundamental components, as summarized and simplified in **Table 2**.

Table 2.

Macro components linking heuristically the domains of biochemistry and mechanics. Examples elaborated from Lejeune (n.d.-a, 1972a, 1972b, 1981a, 1982, 1992).

#	Component	Problem in the mechanical domain	Example in the biochemical domain
1	Network	It is missing or damaged.	Failed development of parts of the brain (as it can happen in Trisomy 13 and 18) due to embryonic stages which have not taken place, or damages happened later due to infections, hemorrhage, ischaemia or compression due to too high pressure of the fluids in the skull.
2	Components	Functioning is disturbed, not precise, due to a lack of insulation that protects the network components against short circuits or undesirable diffusion.	Impossible to effectively regulate the biochemistry of the manufacture of "insulating" substances, leading to the collapse of the network's performance, and the accumulation of substances can even destroy the components. It happens in very well-known disorders of the insulating sheaths, like Tay-Sachs disease, Niemann-Pick disease or Gaucher's disease (all genetic and inherited disorders).
3	Connections	Failure in circuit communication between components that are not physically contiguous, due to disturbance.	In the brain each component (terminal button of an axon and receptor cup of a dendrite) is disjointed, communication happens through the exchange of molecules in the intercellular medium. The synapse space is open for molecules to pass through: terminal buttons and receptor cups change their properties to emit and engulf specific ions in sequence (the chemical mediator, like Acetylcholine, Noradrenaline, Sertoinin etc.), working against entropy, and in this way relaying chemical impulses (Lejeune, 1980). If "parasitic" molecules infiltrate this delicate space, the impulse is corrupted. It is possible to detect functional subsystems in the network, which use a specific common mediator language (motor system, pain transmission, regulation of the mood, etc.). This specificity allows the precise pharmacological effect of some drugs which excite (or paralyze) one particular system and not the others.

#	Component	Problem in the mechanical domain	Example in the biochemical domain
3+1	Speed (timing), as a consequence of #3. Connections	Disturbance slows down circuit communication, resulting in breakdowns of the information chain.	Chemical imbalance in synapses hampers the communication between neurons, requiring even more molecules to compensate and leading to loss of information. Supply and disposal of mediators does not happen at the right time, at the appropriate amount and in the correct location. Biochemical communication takes longer to complete, the speed to open up new communication is reduced. The primary information that had to be analyzed and compared with previous results may already have been lost before this comparison is possible.

Lejeune hypothesizes that the majority of mental disorders correspond to a failure of the third type, a *connection* problem, with a *network* apparently normal and in good condition, operating though at very low efficiency. This low efficiency should come from a mild but continuous intoxication from a substance which they accumulate as a result of an enzymatic blockage in conditions of chromosomal defect, or an excess of enzymatic activity in conditions of chromosomal excess. All in all, it would be as if these people were continuously drugged by the inherent chemical imbalance. The intuition of adopting such a model, even if clearly the analogy with mechanics does not describe the reality, is therefore aimed to guide research towards defining the intimate mechanism of mental retardation, and to discover which “parasitic” substances have to be eliminated through diet or therapies to restore the network normal functioning.

The Machine drawing reports four labels on the borders, each of which can be described with the help of Lejeune (n.d.-b, 1979, 1981b) and it can be related primarily to the set of the four operating conditions of a machine. The relation can be inferred from an article by Lejeune (1980), and it is proposed in **Table 3**.

These first categorizations provide insights from the information design standpoint. The analogical categorization of

the kinds of metabolites presented in **Table 2**, which is qualitative in the biochemistry domain and operational in the mechanical domain, become the very constitutional elements of the visual analogical model of the Machine. Furthermore, the four elements collected in **Table 3** act as the highest level of conceptual categorization of the set of metabolites included within the Machine. Indeed, the reticule generated by the positioning of the labels for the four categories generates a sort of flexible and loosely defined grid that provides a high-level ordering for the positioning of the gears and their grouping in pathways. **Figure 7** proposes an elaboration of this concept.

The main purpose of these categorizations is to provide immediate context to the reader: the boundaries of what is relevant and what is out of scope are provided visually in a perceptible way. This is of course unavoidable in the design of a visual artifact, but what is important is how these categories reflect the high-level decisions of the author on what to focus the attention on within the vastness of the human metabolome (or the primary domain in general). These categories define the *reference frame* (Bonora et al., 2020) of the visualization. The concept of reference frame is elaborated further in Chapter 5, but here we can already state that in information design the reference frame is a graphical and conceptual device that can be described as a *compressed context*, that is devoted to providing the reader with just enough information to activate in their mind the neural pathways aimed to re-enact the full context. The visual and conceptual space of the primary domain of biology is *compressed* by the categorization imposed by the author via the reference frame, it is stripped of all elements deemed in excess or out of scope, and it is presented as a set of visual and conceptual boundaries to the representation. In turn, the readers must decompress this set of choices imposed by the author of the visualization, by resorting to their knowledge, memories and experiences in the domain. What is peculiar to a representation based on analogy such as the Machine, is that it is not easy

Table 3.

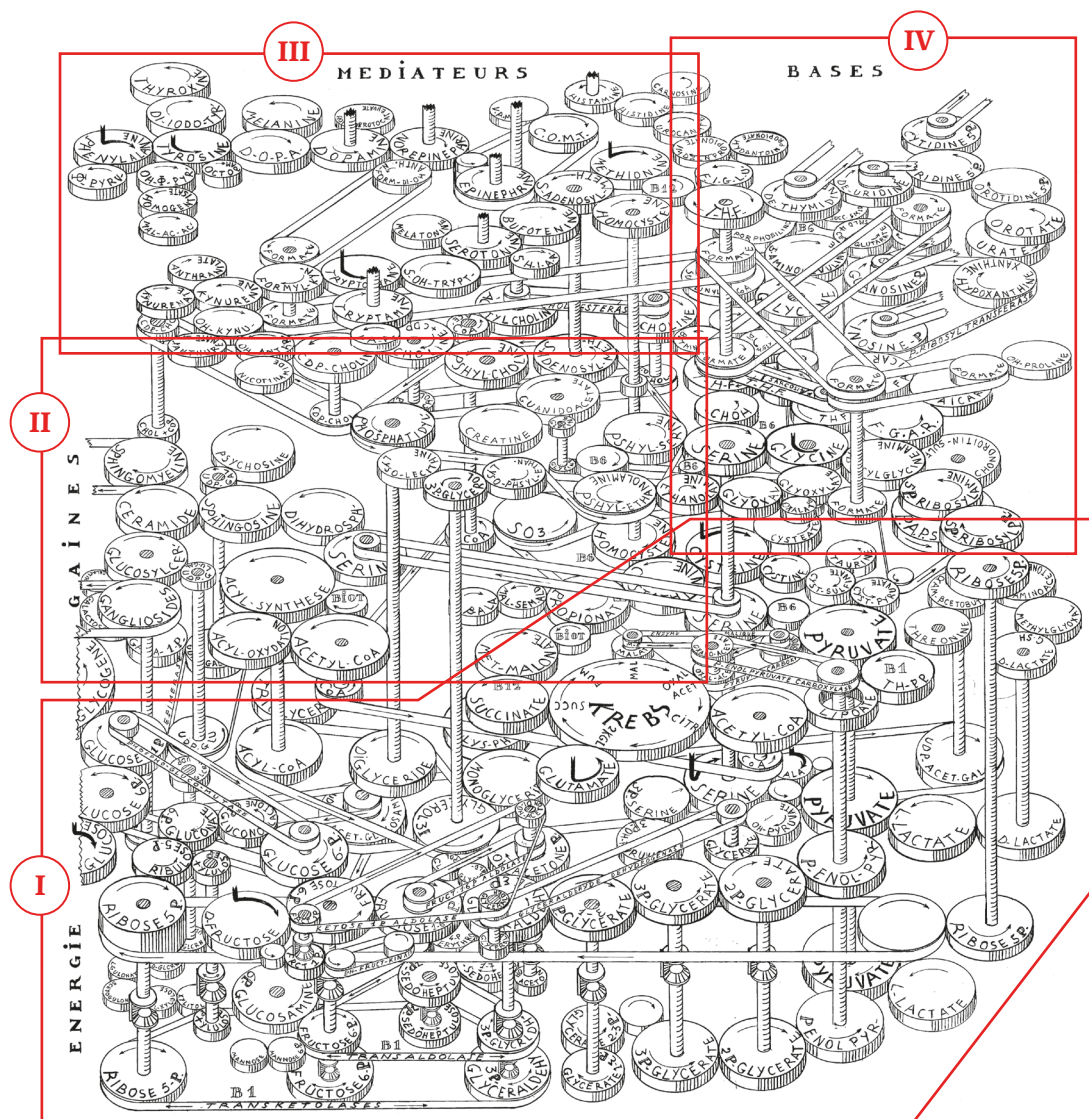
Categorization of elements of knowledge of biochemistry related to mechanics.
Examples elaborated from Lejeune (1972a, 1972b, 1979).

#	Label [FRA]	Label [ENG translation]	Metabolite grouping	Relation with machine operating conditions
I	Energie	Energy	Metabolites contributing to producing the energy via the Krebs cycle and all the feeding and regulating systems around it. This part of the Machine is in charge of making the chemical mediators available at the right place at the right time, so that synapses can transmit and receive the signals correctly.	It supports the whole machine, but it can be related more directly to the "Speed" operating condition.
II	Gaines	Sheats	Metabolites components of insulating sheaths of the nerve fibers, with the addition of the metabolites to manufacture production of the constitutive elements of the membranes (glycoproteins and mucopolysaccharides).	It can be related more directly to the "isolated Components" operating condition.
III	Mediateurs	Mediators	Chemical mediators released at nerve endings, contributing to the correct functioning of connections and intelligence as a result.	It can be related more directly to the "Connections" operating condition.
IV	Bases	Bases	The label stays for "nitrogenous bases", it collects metabolites involved in the genetic makeup of the network.	It can be related more directly to the "Network" operating condition.

Figure 7

Interpretation of the reference frame of the Machine de Lejeune.

The four areas (numbered from I to IV) enclose metabolites related to the categorization proposed by Lejeune (1972a, 1972b, 1979), as summarized and numbered in **Table 3**.



to tell apart anymore if the reference frame belongs completely to the primary or secondary domain, due to the *interaction view* of metaphor (as described in Chapter 4.3.1). The readers must then put a little extra effort into re-enacting both the biochemistry and mechanics contexts in their minds to find their own way towards the elements of knowledge to grasp. The visual and conceptual space is therefore generated as a consequence of the definition of the reference frame and from the way it organizes knowledge visually. Having established the boundaries and focus of the visualization, the navigation of the elements of knowledge within the reference frame can be approached in a visuo-spatial way. This is the key to the information accessibility achieved by a visual representation over a verbal communication (for anyone who can use sight of course), which is enhanced by the analogue nature of the representation in the case of the Machine.

To make a very practical example, while showcasing the poster of the Machine (Lejeune, 1980), Lejeune brings the audience in a conceptual exploration all over the artifact in a series of stages through the overall groupings of metabolites (gears) included within the reference frame, starting from the source of energy: energy enters in the system at the bottom left, where glucose, galactose and fructose are either stored in glycogen or used via the glycolytic pathway toward:

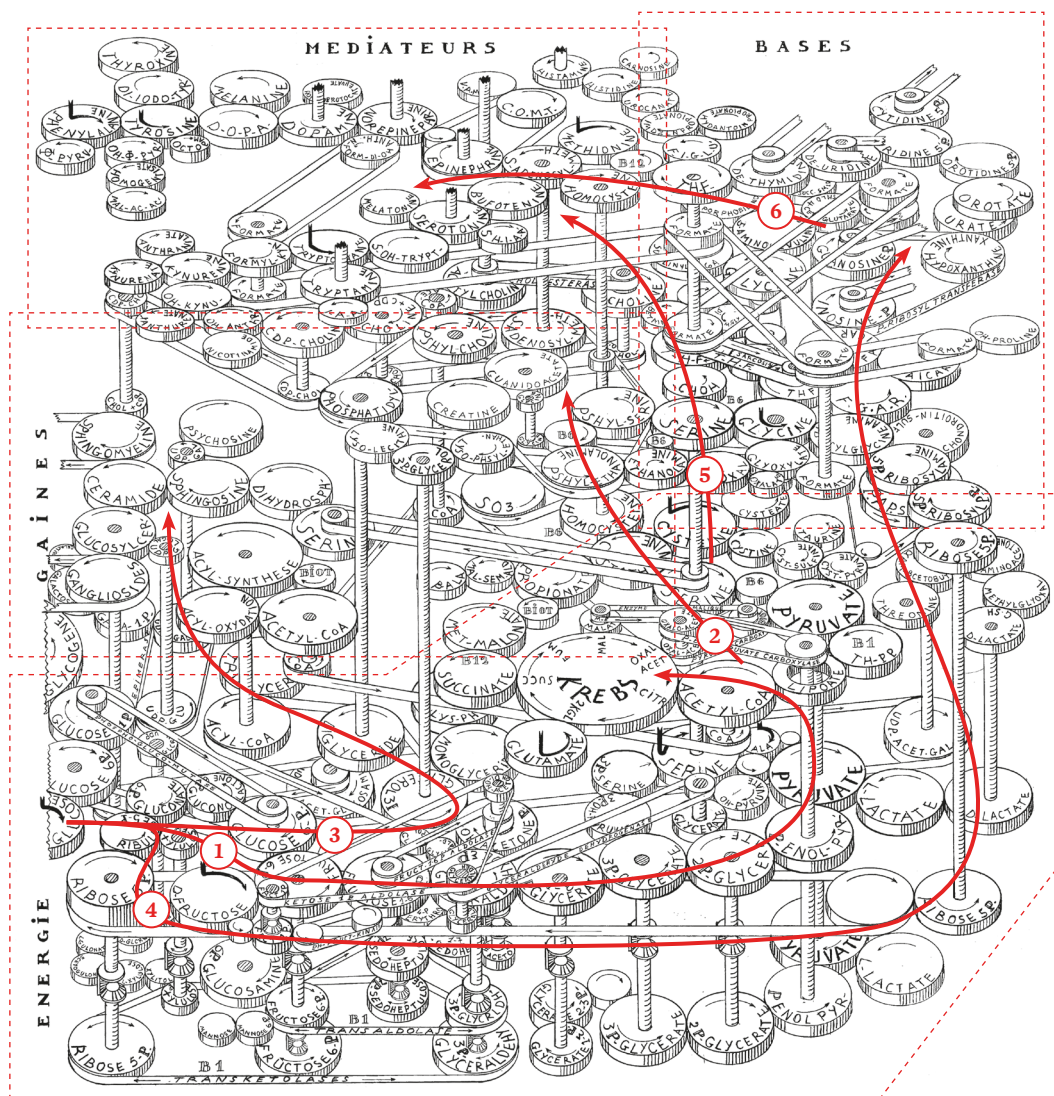
1. the Krebs cycle (the A.T.P. producing dynamo)
2. the production of lipids
3. the insulating substances
4. the synthesis of purine via the hexose monophosphate shunt
5. the production of chemical mediators
6. the regulation process the fabrication of the mediators

This sequence is loosely reconstructed and rendered visually by very general terms in **Figure 8**.

In **Figure 8**, each arrow is numbered to match Lejeune's arguments, and the visual representation proposes a situated example of the direction of visual inspection that the reader

Figure 8

Interpretation of the main pathways of metabolic functions, following Lejeune (1980). A possible visual mapping of the metabolic pathways towards (1) the Krebs cycle, (2) lipids, (3) insulating substances, (4) purine, (5) chemical mediators, (6) regulation processes of mediator production.



can follow to understand (*visualize*) Lejeune's arguments. By no means the arrows represent the exact metabolites which Lejeune implied in the example, also because he expected the specialized audience to already know about those metabolites without him enunciating them one by one. Moreover, the Machine is indeed the representation of the portion of a fully interconnected network of metabolites and reactions happening within human cells. Therefore, even if a main pathway is the focal point of the investigation, all the other reactions are interconnected and still happening at the same time, no reaction is conceived to happen in a vacuum. The general interest still lies in the whole machinery itself.

Nevertheless, if the reader is acquainted enough with the very basics of biochemistry, it is affordable to follow along with the referencing of specific areas of the metabolome. For a researcher, the possibility of being supplied the whole set of metabolites laid out in such a way allows them to assume the very basic level of complexity (the *mapping* component of the discourse) to push forward focusing on seeking out where abnormalities could be (the *heuristic* component of the discourse).

2.4.2. The complexity within the Machine

The Machine is an evolution of the arguments described in Chapter 2.4.1. Indeed, focusing on the conceptual and visual model of a pseudo-pascalian machine, Lejeune takes the position of keeping the model as simple as possible, conceptually and representatively speaking, ruling out more complex electronic representations. This choice is perfectly in line with the notion of acting urgently and using a basic model to direct the research work. The main publications which include direct descriptions of the Machine are from Lejeune (1977, 1979, 1980).

As already mentioned in Chapter 1.2, the basic intuition of Lejeune (1977) is to collect information from three main parallel

sources of scientific research, that are (1) clinical investigation of the affected persons, (2) systematic biochemical investigations and (3) gene mapping. The need to collect information over a single model is what brought the Machine to life, to serve the purpose of representing machinery regulating the production of chemical mediators. Human intelligence is the result of an enormous quantity of morphological and chemical functions which are highly integrated, and the segments of chromosomes involved in cytogenetically recognizable diseases contain hundreds of genes. A heuristic approach is required to direct the attention to the most promising mediators (metabolites) starting from a specific condition, that is Trisomy 21.

Summarizing, this is what the Machine showcases as data: a portion of the human metabolome, which includes a subset of all the metabolites used by the organism, which from preliminary research and clinical observations seem to be more impacting the health (including mental performance) of people with Trisomy 21.

Keeping always present the four fundamental components of the functioning of a machine (see Chapter 2.4.1), Lejeune (n.d.-a, 1980, 1981a, 1982, 1984) highlights what is the result of such strict conditions, and the most important characteristic for his context of use: logic is anti-randomness, a calculating machine is not allowed any variance in its running and its function is to provide a certain path for information that has to be meaningful. Each turn made inside the network must be “yes” or “no”, never “maybe”. By no chance, this characteristic determines the appropriateness of the representation. Of all the possible visual models of a machine, the “machine arithmétique” of Pascal is probably the one which makes this concept the most visible and perceptible. Lejeune (n.d.-a, 1981a, 1982, 1984, 1992) asserts that when Pascal discovered that arithmetic calculus could be simulated by the working of gears and pulleys, he demonstrated that logic can be implemented into aptly crafted matter. This had to be the reason for the choice of Lejeune to start from such

representation. Indeed the geometric invariance of gears and bars within the Machine does not allow for variance, it implies logic. Each component should match the others and run as intended following its construction.

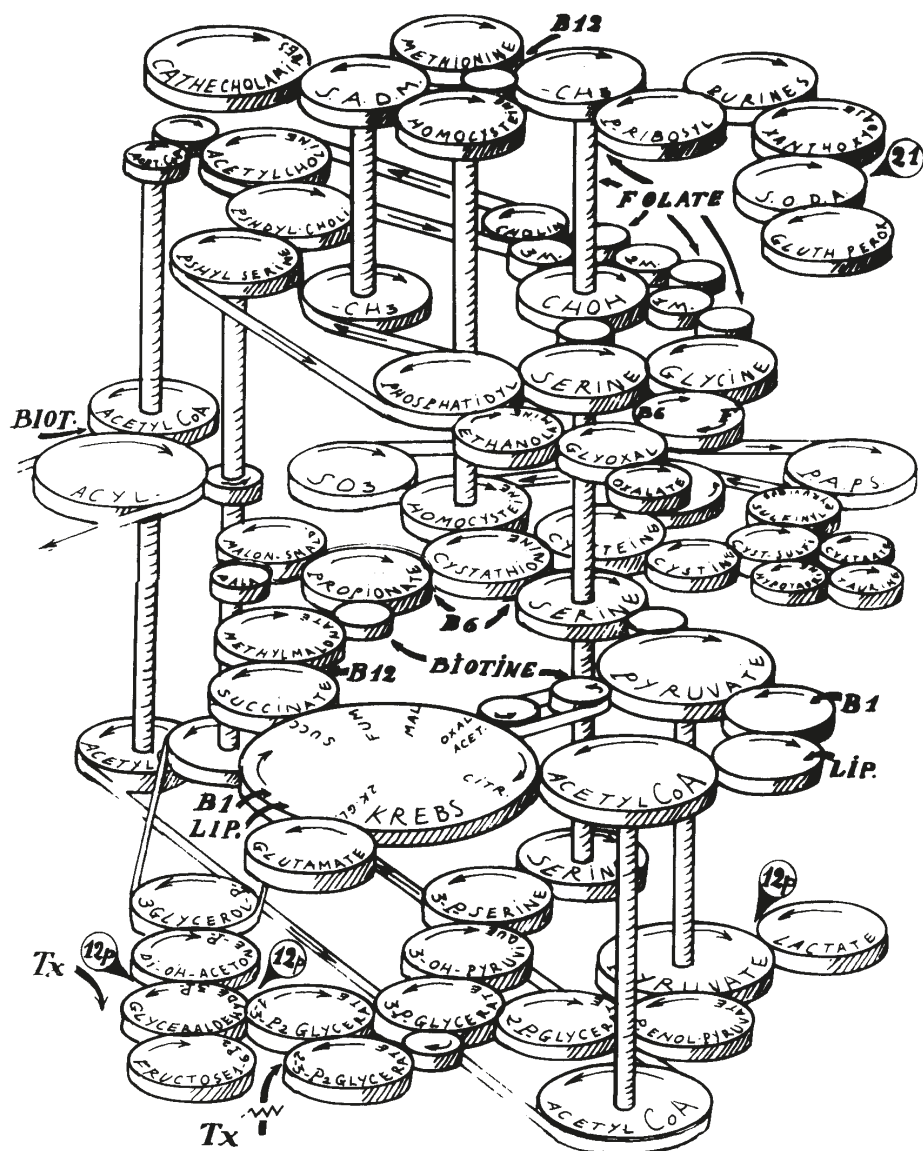
The expected regular behaviour of components allows the reader to focus on a specific part of the Machine, filtering out metabolites (gears) which become peripheral to the specific and narrow focus of interest while not violating the general principles of the visualization. In a smaller version of the Machine (Lejeune, 1977, see **Figure 9**), Lejeune showcases only some metabolic pathways focusing on key aspects affecting especially children with Trisomy 21: (1) the constitutional deficiency of the cholinergic activity, causing the typical symptoms of Down's syndrome like hypotonia, chronic constipation and visual accommodation difficulties (Lejeune, 1979), possibly due to the slower release acetylcholine or due to some impairment in the manufacture of this cholinergic mediator; (2) the steps related to the glycolytic process that are slightly accelerated as well as some excessive amount of some amino acids. Lejeune points out the areas in the scheme where the reader can find relevant metabolic pathways and reactions, which are proposed visually in general terms in **Figure 10 (right)**.

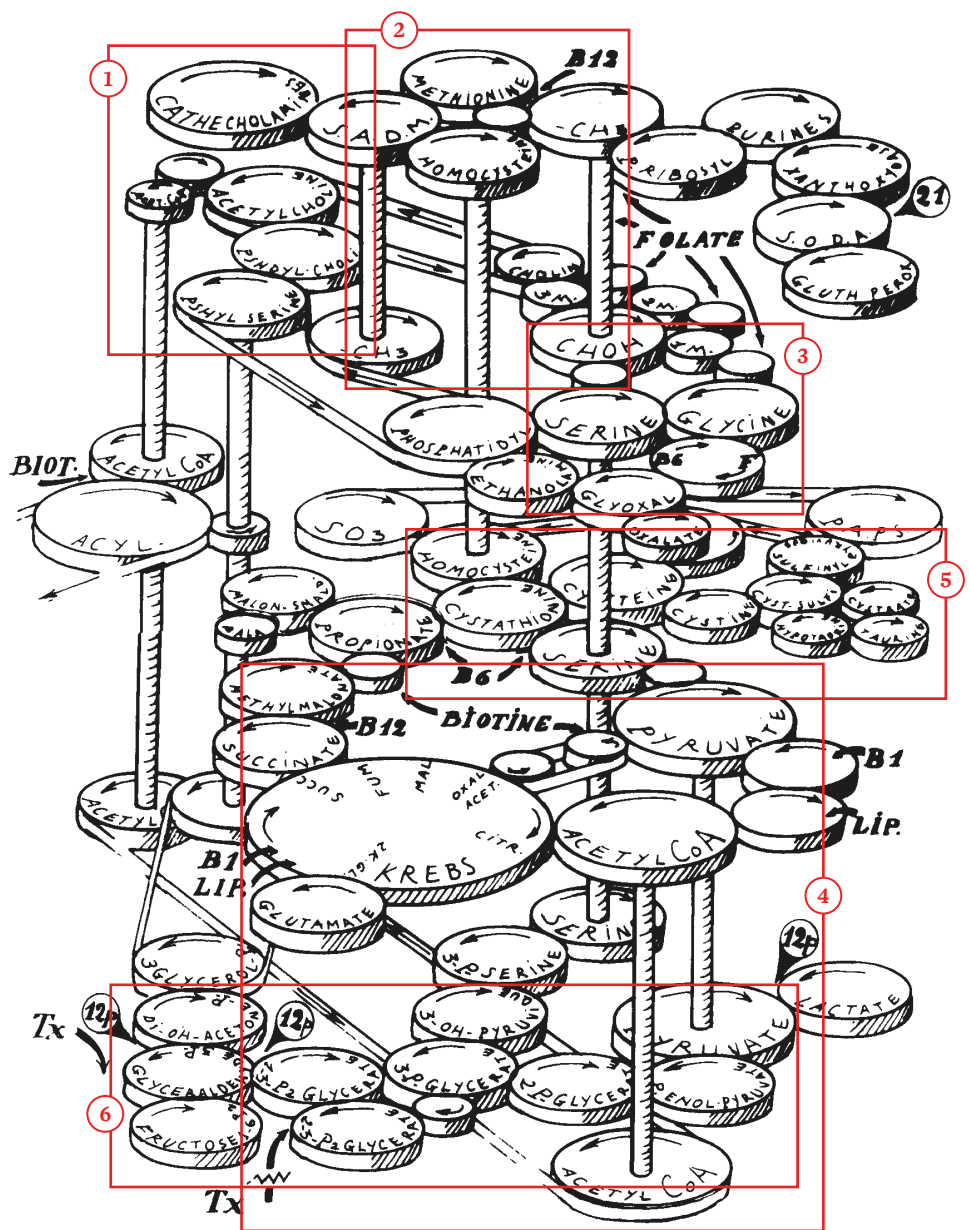
The partial version in **Figure 9** predates the complete representation of '78 in terms of publication, even though it is evident that both are products of the same principles and way of thinking. It is of course possible to trace the relation between the two versions, the partial one is more synthetic but it is still possible to trace each metabolite and to map it in the complete version **Figure 10 (left)**. The two visualizations do not match exactly, since they have two different focuses.

It is interesting to note that it does not actually matter whether the partial version was developed before the complete one or vice versa, since they both obey the same principles: reducing the scope of the visualization focusing on a specific aspect, or expanding it to embrace the whole machine, it does not

Figure 9

Scheme of the "chemical machinery" for adrenergic and cholinergic mediators. Retrieved from Lejeune (1977). The numbers in the bubbles represent enzymatic blocks known in specific genetic conditions (trisomies 21 and 12p), while arrows point to specific enzymatic reactions (Lejeune, n.d.-b).





compromise the analogy and the visual device. The operation involves managing quantities, either suppressing the metabolites-gears motion out of scope while justifying and assuming the remaining ones, or adding more metabolites-gears quantifying their reciprocal motion.

2.4.3. Heuristic value of the model - Directing the sight

Creating a general model which can be conceptually filtered on need, as shown in the previous chapters, opens up to propose hypotheses by making heuristic use of the model itself. Lejeune is always aware and clear about how limited the heuristic approach and the representation of the Machine can be, both due to the complexity of the domain and to the fact that reasoning by analogy imposes a series of hypotheses (Lejeune, 1979). However, the model is the means by which pathogenesis can be compared across subjects and conditions, from experiments, clinical observations and phenotypic manifestations. Here lies the core power of the proposed heuristic model: mapping imbalances in metabolism is functional to a multitude of potential goals. Investigation of Trisomy 21 is just one way to interrogate the model.

If thus detected by the logic of the chemical machinery, the metabolic shifts could be tested one by one, the insuperable difficulty actually encountered being not the technicalities of the research, but the very lack of indication of where we should look for. (Lejeune, n.d.-b)

Indeed, Lejeune (n.d.-a, n.d.-b, 1979, 1981b, 1981a, 1982, 1990) highlights how different genetic conditions leading to neurological disorders and mental deficiencies, correlated also by some morphological traits in the person and clinical profiles, show chemical imbalances on elements that are

relatively close in the Machine. **Figure 11** showcases a version of the Machine (from Lejeune, 1982) on top of which Lejeune marked the enzyme blockages of known conditions affecting mental functioning. At the beginning of the '80s, the scientific discoveries of Smithells and Laurence on the relationship between low levels of folic acid and Spina bifida or anencephaly shone a light on the importance of this vitamin during pregnancy (Lejeune, 2002, p. 101). By reviewing literature in the field and looking at the Machine, the intuition that Lejeune brings up is that disorders in the metabolism of monocarbons (radicals containing only one carbon atom) entering the folate metabolism cycle (Tetrahydrofolate [THF], the active form of folic acid) seems to be involved in most of the enzymatic blockages causing mental retardation. This seems particularly plausible without other demonstrated abnormality of the cell membranes and nerve sheaths, and without major anatomic defects of the brain and its genesis. Variance in the manifestation of mental deficit across conditions sharing this poor metabolism of monocarbons is probably due to patients compensating for the deficit in one input by accelerating the others, keeping a balance.

Interestingly enough, inspection of the machine shows that all these various conditions could have a common consequence, a disturbance of the one carbon cycle. (Lejeune, 1981b)

Lejeune (n.d.-a, 1981a, 1982, 1984, 1990) describes how monocarbons are the smallest building blocks of the cerebral network and they are also the most frequently used molecules in many areas of the metabolism. The general heuristic hypothesis about monocarbons is that deficiencies in the supply of their precursors, or their transport (folate cycle) or their appropriate usage (methyltransferase) could play a key role in metabolic disruption. To make a quick example (Lejeune, 1984, 1990, 2005), amongst a number of functions the monocarbons serve, the insulating substances of the nerves are essentially

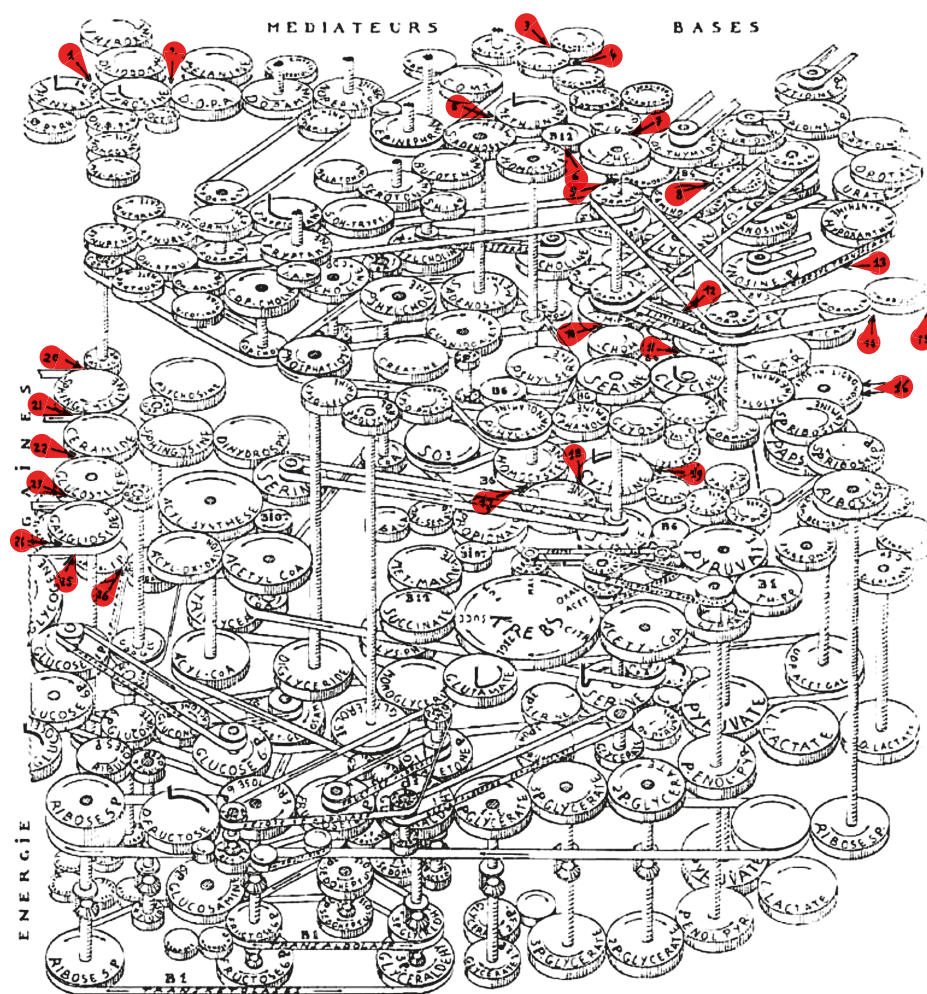
phospholipids made of three methyl groups (in general, three monocarbons groups), they are fundamental to tubulin (which constitutes the neurotubule network) and bipterin (fundamental to manufacture mediators like serotonin, catecholamines). To manufacture the DNA or RNA there is the need to manufacture purine (two monocarbons per molecule), pyrimidine and timine (one monocarbon). Folic acid and vitamin B12 are the transportation system of monocarbons, driven to build the cell nucleus and neurons, whose deficits lead to severe mental deficiency and neuropathic diseases. **Figure 13** shows an elaboration of the diagram from Lejeune (2005) which groups the main pathways involving monocarbons.

This important metabolic cycle is indeed being investigated further these days as well by the researchers at the Laboratory of Genomics (see Chapter 6.1). The research community in biochemistry and medicine (Ducker & Rabinowitz, 2017) is still very much interested in the folate metabolism, which supports the broader set of transformations of the monocarbons metabolism, as there is evidence that problems in this pathway create a disposition to birth defects in the neural network of the developing fetuses. **Figure 12** roughly delimits the areas in the Machine which focus on the metabolic pathways around the monocarbons cycle.

Figure 11

Visual elaboration of enzyme blockage scheme from Lejeune (1982).

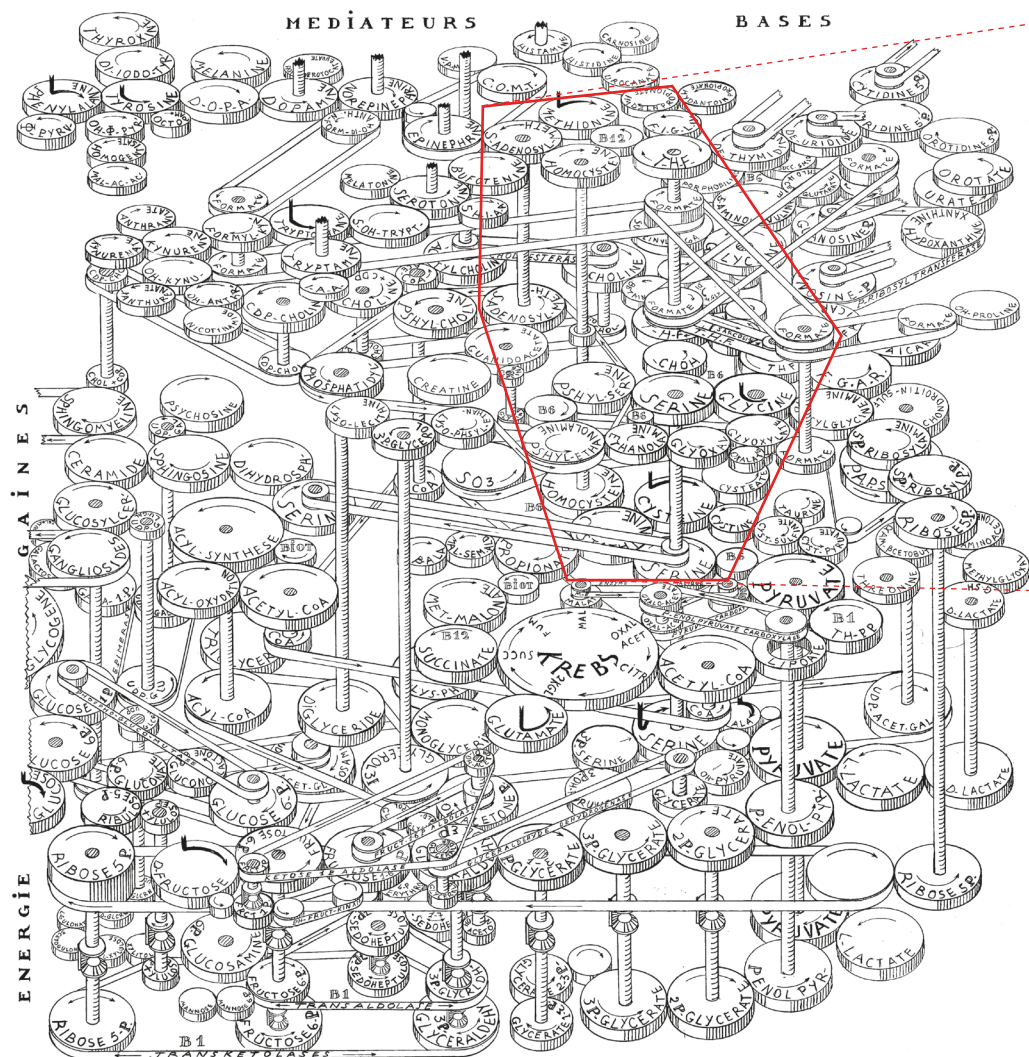
The blockages correspond to various genetic diseases involving mental deficiency.

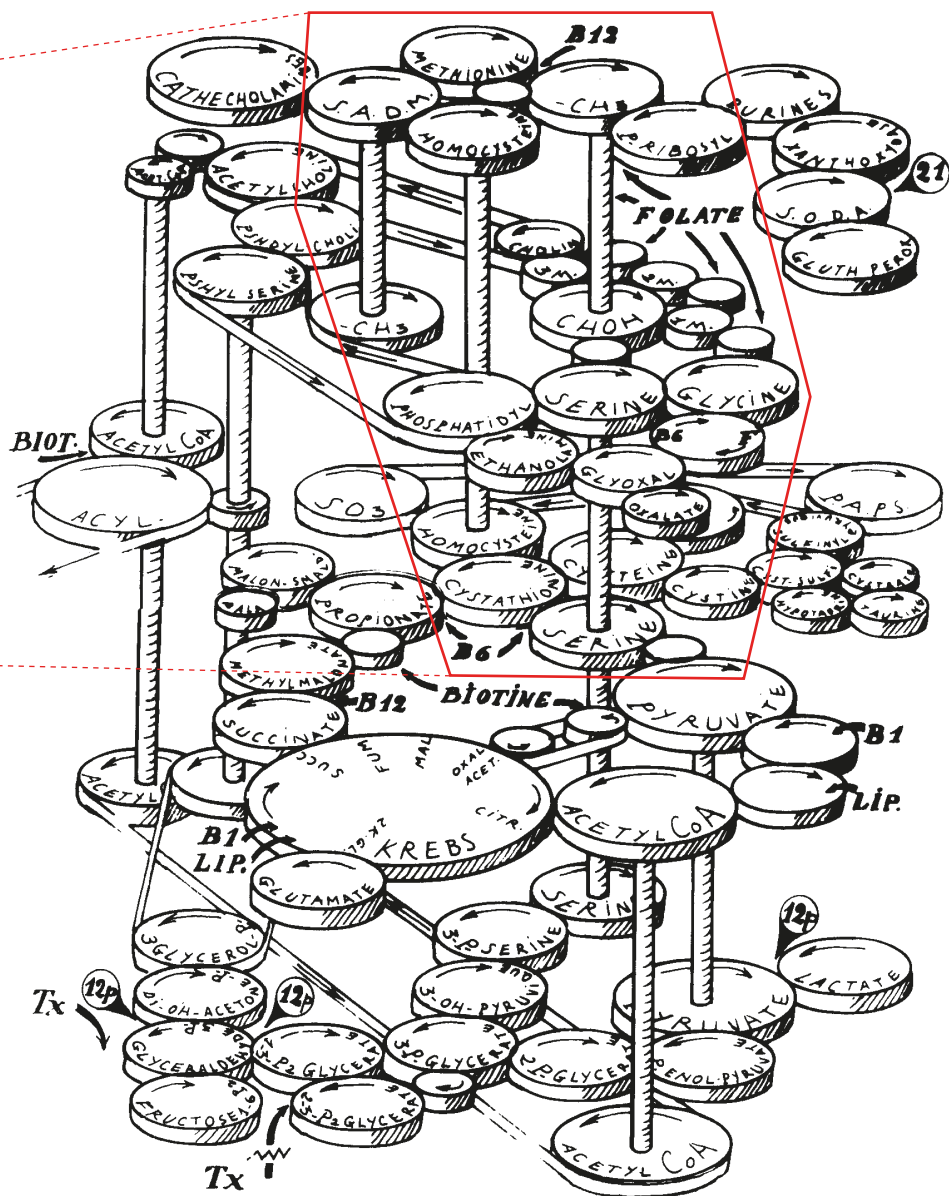


Note. (1) Phenylketonuria; (2) Tyrosinosis; (3) Camosinemia; (4) Histidinemia; (5) Hypermethioninemia; (6) Deficiency of vitamin B12; (7) Formiminotransferase deficiency; (8) Porphyrria (and 5-aminolevulinate-pyruvate transaminase deficiency); (9) 5,10-Methylenetetrahydrofolate reductase deficiency (and other Folate cycle deficiencies); (10) Serine hydroxymethyltransferase (SHMT) deficiency; (11) Glycine decarboxylase deficiency; (12) Sarcosinemia; (13) Hypoxanthine-guanine phosphoribosyltransferase deficiency; (14) Hyperhydroxyprolinemia; (15) Iminodipeptiduria; (16) Mucopolysaccharidoses; (17) Homocystinuria; (18) Cystathioninemia; (19) Beta-Mercaptolactate-cysteine disulfiduria; (20, 21, 22, 23, 24) Diseases of the insulator substances, involving myelin; (25, 26) Galactosemia.

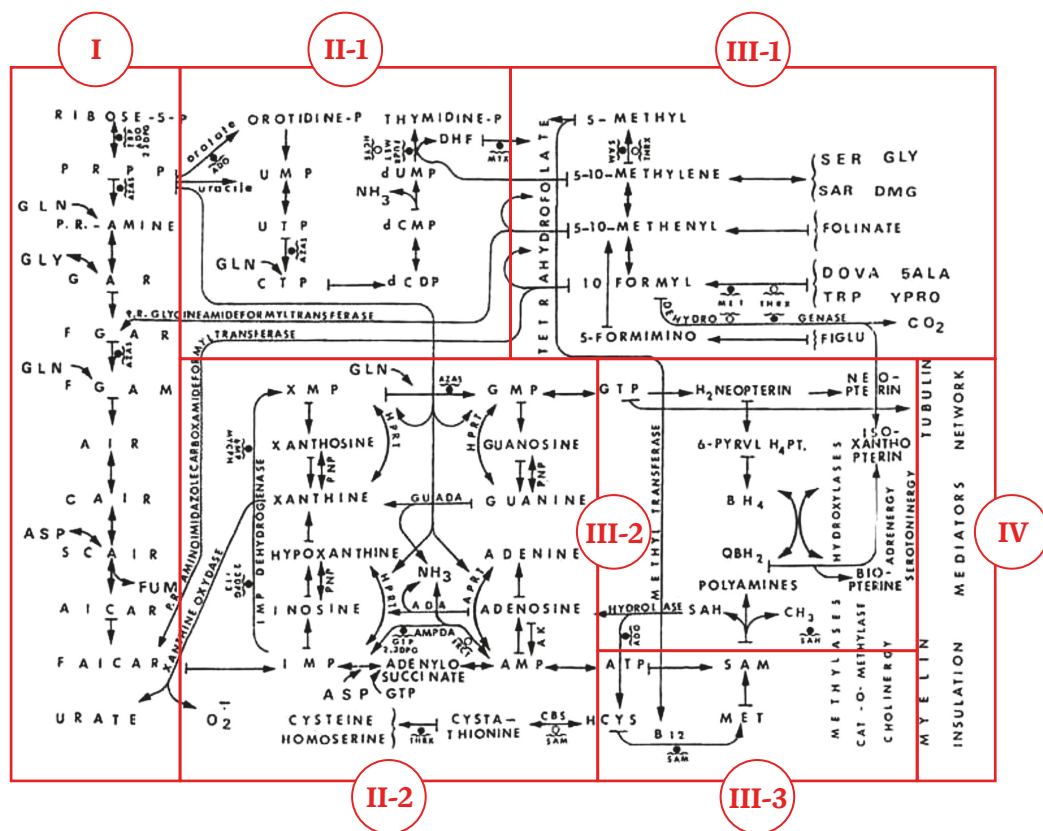
Figure 12

Elaborations on the complete and partial Machines, highlighting the areas focusing on the one-carbon cycle.





Biochemical pathways involving monocarbons which impact on intelligence.
Elaboration on the diagram from Lejeune (2005).



Note. Pathways grouping: (I) purine synthesis; (II-1) pyrimidine and (II-2) purine interconversions; (III-1) folate and monocarbon metabolism, (III-2) bioprotein and hydroxylases), and (III-3) methylation; (IV) products for the informative network (tubulin), a gating process (chemical mediators) and an insulating system (myelin).

It is worth reporting some implications of this focus on Trisomy 21 and especially around the monocarbon cycle, since it involves another kind of visualization Lejeune proposed (**Figure 14**), comparing it to the visualization of the Machine.

Lejeune (1979) enlists diseases where certain phenotypic and biological symptoms are especially peculiar to people with Down's syndrome, in the attempt to identify which metabolisms might be deviated. Amongst the description of typical conditions, Lejeune hypothesizes how an anomaly of oxygen metabolism in Trisomy 21 can impact several of the traits which characterize the syndrome: collagen and elastin disorders, deficits of the THF inputs to the monocarbon cycle, and cholinergic deficiency. What is known is that the excess of Superoxide-Dismutase-A accelerates the reaction $O_2^{\cdot-}-H_2O_2$. A deficit in superoxide ion ($O_2^{\cdot-}$) could reduce the yield of reactions incorporating an oxygen atom into a molecule, while excess production of hydrogen peroxide H_2O_2 could imply the abnormal working of several reactions also involving $O_2^{\cdot-}$, which remain consistent with the indications drawn from the pathogenesis and comparative pathology. The scheme in **Figure 14** replicates a map from literature (a notorious biochemical atlas, by Michal, 1974) by adding indications of where the oxygen molecules and reactions involving $O_2^{\cdot-}-H_2O_2$. Lejeune hypothesizes that the reactions marked with the “crossed circle” sign could then be slightly slowed down.

Without going further down in biochemistry details, the analysis of the link-diagram schemes in **Figure 13** and **Figure 14** helps us to make some further considerations and comparisons from the visual design side. Lejeune uses both of the schemes as reference and notation for the narration of his hypotheses. He arranges and groups information while adding further contextual notes to direct the readers' sight to specific phenomena (pathways). Both the schemes report knowledge of the expected behaviour of functioning metabolic pathways, and Lejeune uses them to map the scope in the biochemistry domain which

he believes is the most relevant or promising. The notation purpose, the choice of information to represent and the scoping of the schemes are similar to the ones of the Machine. Moreover, these characteristics end up attributing a heuristic value to the schemes which is conceptually similar to the one of the Machine: to support finding metabolic pathways which behave divergently. What fundamentally changes between these link-diagram schemes and the gear-like Machine is their visual presentation, which impacts the accessibility of the information.

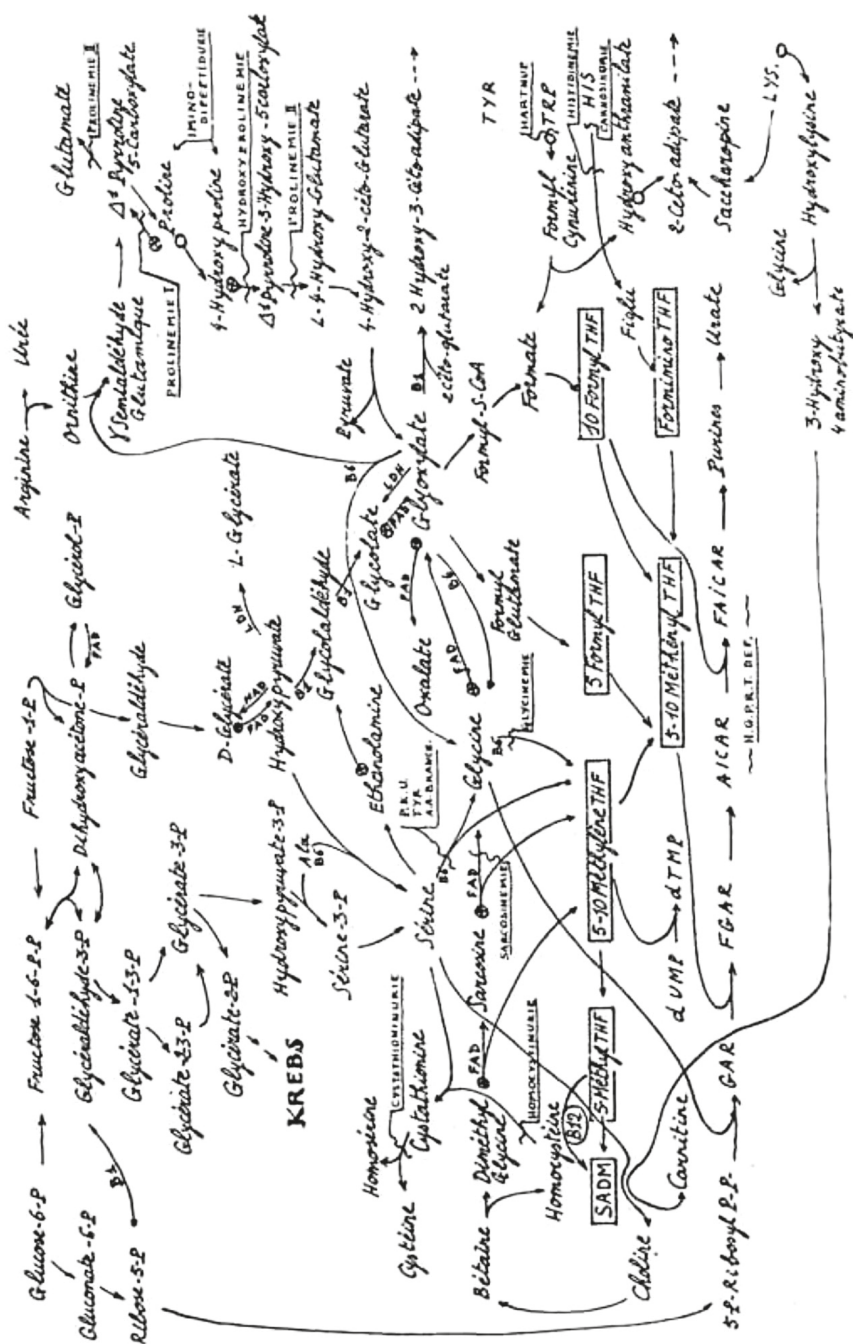
To the readers' eyes and mind, the representation in **Figure 14** demands following one by one the links, in a procedural way, to rebuild the whole structure of the network of metabolites. While advancing procedurally, the reader needs to keep in mind the previous subnetworks, and to bounce around the scheme up to the point they know more or less by heart where the information is located. There are no perceptible supports for the mind to hook up to, to "bookmark" and fast travel to the information on need, except for some features, like the bold text for the centrally important KREBS cycle or the rectangle containers for the metabolites involved in the monocarbon/THF cycle. The eyes are free to roam on the page, whereas the Machine proposes an emerging structure to figuratively *walk* onto.

Figure 14

Simplified diagram of the metabolisms discussed by Lejeune (1979).

On the next page.

Note. The "circle" sign indicates the incorporation of one or more oxygen atoms. The "crossed circle" sign indicates the concomitant reaction of O_2^{2-} (superoxide ion) and H_2O_2 (hydrogen peroxide).



The Machine visualization makes it easier to perceive that the metabolites possibly involved in anomalies of oxygen metabolism in Trisomy 21 can impact more the pathways related to energy production, and also the THF (folate) and one-carbon cycles (compare for example **Figure 9**) reaching the bases for those cycles and the mediators resulting from them. All this information is accessible more or less at a glance.

The same considerations can be made for **Figure 13**. Although the two-dimensional information is arranged in a more orderly manner through the planar position of the labels—so that Lejeune can even describe a sort of reference frame through grouping criteria—the reader must always follow with the eyes the network of links in a procedural way without an explicitly described basic structure to relate to. From these comparisons, emerges the key strength of the analogical representation of the Machine: its capability to make information perceptible and to create a structure in the visual space that has an explicit meaning.

From this comparison, it is also worth noting that the original source of the scheme in **Figure 14** (Michal, 1974) predates the Machine by three or four years. The knowledge of biochemical pathways at the time was already well developed, and almost certainly Lejeune started building the representation of the Machine taking these kinds of schemes as reference. The logic of linking together the sequences of metabolites and reactions on a two-dimensional plane is ported by Lejeune in the imaginary three-dimensional quasi-isometric space of the Machine by the concatenation of gears. Both the representations include some conventions which do not make them one the perfect mirror of the other. Nevertheless, this is something that an experienced biochemist can overcome by simply reading the labels and remembering the fundamental metabolites involved in the pathways. Indeed, Lejeune uses the Machine as a way to describe and hypothesize over the findings he is collecting from previous literature, trying to bring everything together on a single model.

3.

Rhetorical devices in design

Design literature often mentions the usefulness of rhetorical devices such as metaphors and analogies for establishing compelling conceptual models for the information architecture and design of interfaces and visual artifacts. However, the literature in the design field seldom provides descriptions of analogy and metaphor which support the designer in identifying and exploiting the useful features of these logical devices. Knowing more in-depth about the logical implications of using analogy and metaphor while preparing visual artifacts, especially for scientific use, could prove to be an important addition to the skill set of designers.

In this chapter, I will discuss pointers from relevant design-related literature, while in the next one, I will add information from fields that deal with rhetorical devices and representation in close connection with scientific practice. This collection of multidisciplinary input should provide the reader with a series of open questions and tentative answers capable of adding new content to the discipline of design.

3.1.

Design, research, science

In his brief history of ideas behind UI metaphors in Human-Computer Interaction (HCI), Blackwell (2006) remarks how HCI textbooks and even commercial software design guidelines advise, more or less synthetically, to employ metaphors in the design of a system when possible, especially ones familiar to the User. Rarely though the guidelines extend much further. Nevertheless, it is now established in the HCI discipline the recognition of metaphors as a creative tool available to the designer. This awareness comes more from a historical and developmental perspective on the topic of conceptual and mental models rather than a precise set of theories that are considered established.

The author traces the history arch leading to modern Graphical User Interfaces (GUIs) which also incorporate metaphors. The practice of creating integrated project teams to solve technological problems was first grounded in military tradition, with teams more interested in human factors and cognitive demands placed on the operator. This tradition was ported to corporate research laboratories of firms such as IBM and Xerox. Over the years innovations in GUIs were driven by designers cultivating interests in hardware and software techniques, shaping UIs through intuition and user testing to define requirements. However, modern GUIs have not arisen out of natural usability principles, but rather from a continuous series of innovations. Direct manipulation within the GUI was one of the most enabling features for the design of UIs, but it was not made readily available at once. Steps along the realization of direct manipulation involved the development of functionalities such as the selection of an object through a pointing device, the introduction of pictorial icons to represent relations, the relocation of graphical objects through *drag and drop*,

the text insertion using a cursor between characters, and so on. All these features contributed to form one of the first pervasive metaphors in GUIs, the *desktop* one. Around those same years, in the '80s, scholars from cognitive science, anthropology and education traditions produced works investigating metaphors in theory and in application, which became influential in the HCI research community. The work from Lakoff & Johnson (1980) became peculiarly relevant due to their reflections on the pervasiveness of metaphors in our vocabulary and their relation with bodily experience and mental images, all topics which are of great importance for HCI. The accounts of theories from cognitive psychology, education and linguistics eventually led the HCI community to develop the concept of *mental models*, an attempt to an objective, formalizable, and symbolic description of user's understanding. The reification of a metaphor in graphic terms opens a visual communication channel through which the designer rapidly transfers a model towards the users' cognition, providing the users with a means to access the information. At the same time, the appropriately designed metaphor enables expert users to bypass the metaphor if they already possess the necessary information.

The concept of *mental model* still holds up today, and it is paired with the concept of *conceptual model* (Johnson & Henderson, 2012), which is a high-level description of the system. Ideally, if the mental model and the conceptual model match enough, the user is “attuned” to the information system and understands the relationship between information. Nevertheless, if it is manageable to produce a description of the information architecture on the system side, what is fundamentally unknown is the organization of knowledge in the user's mind, their mental model. Any formalization of a mental model is barely a rough representation of the infinite complexity of the cognition of the user. This breach between mental model and conceptual model is where metaphors find the occasion to ease or alter the user's understanding.

If metaphors can support the conceptual dialogue between designers and users, metaphors can be part of the process of creative design, as a means to dialogue between designers. As Blackwell (2006) points out, literature in the field highlights the value of metaphor and analogy in supporting designers to achieve creative intuition, and that perhaps the greatest benefit from using metaphors might be experienced by system designers while conceiving the product more than the users while using it. Yet, as much as this concept is acknowledged and shared within the HCI research community, there is no theory of interface metaphor. The concept of metaphor is still a “complex aggregate of design concepts borrowed from technical literature in cognitive science, education, philosophy, and the design of computer displays and control interfaces. The technical heritage has been reified in designed products, incorporating the many incremental inventions of object-oriented direct manipulation. [...] the technical literature has been supplemented by a large nontechnical literature”. The author remarks that even though all this input from the literature provides a scientific basis for the notion of perceptual and mental benefits of UI metaphor, they have never been more than partial explanations. Accounts of theory-based design can be found in any of the disciplines that have constructed rich accounts of metaphors (e.g. philosophy, linguistics, rhetoric, etc), but they will always tend to provide analytic tools to deconstruct design concepts into structural components and relations. Less is known about the generative process of effective metaphor, which seems to remain more of a single discovery based on the designer's common sense and less on a systematic design process.

This dissertation goes in this direction of collecting inputs from various areas of research, to provide analytical tools to the designers while studying given metaphors or conceiving one. The resulting process is not intended prescriptive, rather it is dialogical with the problem and inclusive in the metaphor conception of its receiver in the most meaningful way possible.

This, however, does not exclude the intrinsic characteristic of metaphors of being born in the mind of the author in a seemingly unexpected way. The Machine de Lejeune is an unicum also because of this.

The endeavour to collect inputs from various disciplines follows what Cross (2007) suggests, that is to “construct a way of conversing about design that is at the same time interdisciplinary and disciplined”. I support that there are ways to apply knowledge that are peculiar to the awareness and ability of a designer, due to the context of application of this knowledge that does not always overlap fully with the sciences and the arts. I am too deeply convinced that design must not completely ignore either the sciences or the arts, given their stronger histories and traditions of inquiry, scholarship and research than design, and upon which designers should draw appropriately while building design's own intellectual culture. On the other hand, I argue against the author's affirmation that there are *forms of knowledge* peculiar to the awareness and ability of a designer. Indeed, by examining the literature reviewed in this dissertation I strongly advocate that the efforts of a scientist such as Jérôme Lejeune in shaping and presenting information could warrant him the description of being an information designer in his own right (as much as any other scientist who employs visual representations to create fruitful pathways to scientific discovery). Most likely these scientists are not fully aware of the *designerly knowledge* (quoting again Cross, 2007) which leads them in the design of their artifacts. Nevertheless, the ability to produce knowledge by making use of visual artifacts is undoubtedly present in any researcher who deals with the management of information, it is not exclusive to design. Rather, it encompasses practices from hard sciences into design. By extension, this is why Flusser (2003, pp. 27–31) calls *designers* those people who could predict floods and draughts of the Euphrates river in Mesopotamia and indicated where to dig new irrigation canals on clay tablets: the ability to look through time

and to represent what is perceptible of the future, and to convert it into immediate actions, is the perspective of the designer. Undoubtedly, this is what Lejeune and other scientists did with their models. As Flusser (2003, pp. 1–6) indeed points out, the distinction between the two branches of culture, the scientific one (quantifiable and *hard*) and the artistic one (qualifiable and *soft*) was overcome in the XIX century, and the design found its place in the breach between these branches acting as a bridge. Design is the avenue in which arts and technique coincide (together with their scientific and critique methodologies), paving the way to a new form of culture. The design of an artifact, meaning the intent infused by its ideator in the form and realization of the artifact itself, is the factor that underpins and adds value to the art and technique alone.

Extending again from Flusser (2003, pp. 7–16), giving shape to a visual artifact (to “inform” it) imposes choices that not only give shape to the elements of knowledge, providing order and structure to an otherwise amorphous set of concepts but also deforms an *ideal* concept of the representation itself. There is no way to conceive an *ideal* artifact, but only one that follows the ideator's intent. Science is a formal endeavour, it works for the definition of models, and the shapes of the artifacts are the containers for such models. The matter cannot be visualized unless it is in-formed, and once it is (in)formed it starts to appear, it becomes a phenomenon on its own. The subject of design is the modality through which forms appear.

The Machine is a subject of design because Lejeune challenges the way biochemistry represents the metabolism, following his scientific intuition, ethical stances and practical necessities. Undoubtedly, he provided shape to more than a formalized set of quantities, he brought into the public debate and in his research domain a different form of visual culture. A visual culture which is conscious of dealing with delicate but fundamental problems, about health, about people, about care.

3.2.

Metaphors for conceptual modeling

In the literature of the information and interaction design research areas, metaphors are often described as important (if not fundamental) parts of the conceptual models underlying interactive systems. Synthesizing from Johnson & Henderson (2012, pp. 17–22, 53) a conceptual model is a design tool, a high-level description of a system, which usually includes all the concepts/objects that the users can encounter, their relationships and how the concepts fit into the tasks that the users can perform within the system. Since it is a schematization of concepts and relationships (e.g. container–content, father–child, branch–leaf, etc.), a conceptual model can relate to other models, like for example the functioning of everyday physical objects. In this case, often the conceptual model includes analogies or metaphors to accelerate learning and to support the interface use by leveraging people's presumed knowledge and familiarity with those objects. Some widely known examples of metaphor-based conceptual models are the computer *desktop* showing metaphors with a physical paper-based office (with its files and folders), or spreadsheets showing arrays of cells, analogous to the cells of paper spreadsheets. The authors warn though that it is evident how analogies and metaphors are limited and inexact, and that when the objects, attributes, and operations of the reference conceptual model don't match with the analogous one, users must be made aware of the discrepancies. However, how to handle these conceptual discrepancies is not debated further by the authors.

Blackwell (2006) clarifies how for as much as a metaphor is supposed to be familiar to the users, it is not necessarily experienced as being intuitive at the time of its introduction. This happened for example at the time of the introduction of the desktop metaphor GUI, in the '80s. For many users at the time

the metaphor was extremely confusing, with windows, icons, and direct manipulation all proving frustrating. There was no *a priori* inherent cognitive advantage from these basic operations of pointing, selecting, and moving icons. Moreover, it is clear that the development of the desktop metaphor was not directly motivated by a coherent theoretical view of metaphor, rather it was the product of technical evolution and the historical contingency. But this is not all for the worst: as also Blackwell mentions, the works from Black and Hesse (see Chapter 4.3) propose a conception of metaphor and analogy which is not rigid. The meanings of the elements put into relation by the metaphor shift in light of the relation itself. New meanings are formed in the interpretation process, producing new insights leading to new learning. Users' interpretations are unpredictable, they escape the control of the designer's intent. Users will always assign their meanings for dissimilar elements, not always following systematic and consistent mappings of the kind recommended in HCI textbooks. Conversely, users treat metaphorical meaning as fuzzy, mutable, dynamic and social, which is the fundamental threat to the concept of "objective and formalizable mental model".

We can argue that the attributes of a metaphor of being mutable are what supports more the designer in the conception of the metaphor itself (as also discussed by Max Black), even if these characteristics make it even harder to expect determined inferences from the users' mental model. Without the possibility of dialogue with the users, the designer must take calculated risks of generating misconceptions and misinterpretations. This is particularly problematic in cases of products, artifacts or UIs for a large and indiscriminate customer base. Nevertheless, the need for the designers to keep the modelling for a metaphor open to dialogue and unexpected interpretation is intrinsic to the rhetorical function that the metaphor plays. It is unavoidable, therefore it is beneficial to acknowledge also the possibility of reshaping the elements included in the metaphor to suggest

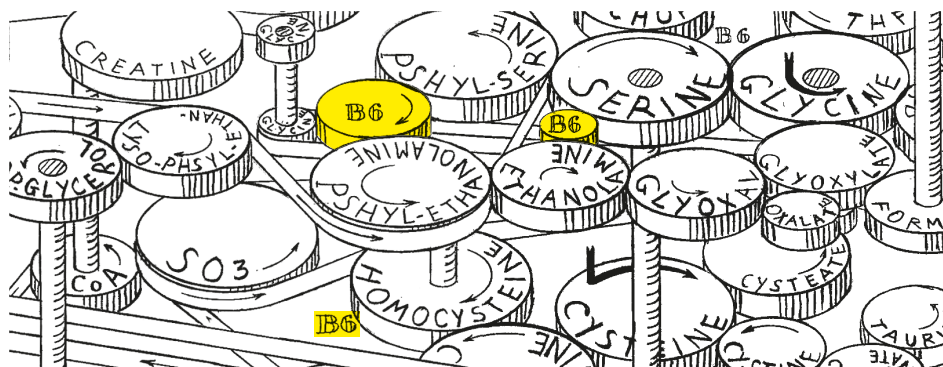
particular interpretations even if they are not structurally coherent within the overall conceptual model.

To make an example on the Machine de Lejeune, let us take a look at the size of the gears (Figure 16). Their radius should be somewhat related to the expected quantity of the metabolites, but in a way that does not comply with the basic rules of mechanics. Molecules expected to be in very small concentration, such as coenzymes (e.g. vitamins), are smaller than other gears with greater concentration, sometimes up to the point that they are not even represented as gears altogether (only as typographical notation). However, the speed of the motion of the gears is the variable describing the reciprocal concentration of contiguous metabolite gears, the ones with less motion (less concentration) should show a bigger radius (much bigger in proportion). This of course if the analogical representation had the ambition to exactly match the two domains and to work precisely as a fully functioning mechanical machine.

Figure 16

Detail of the representation of vitamins in the Machine de Lejeune.

Vitamin B6 is represented with a smaller gear even though its movement should be slower than its contiguous gears. B6 is also not represented as gear but as notation.



The result would be a bit counterintuitive for the reader naive in mechanics but knowledgeable enough in biochemistry: all the molecules with very small concentrations would receive a graphical representation that is disproportionately more impactful than the metabolites which quantitatively are much more relevant. Without direction from the author of the metaphor, the reader is left free to meander in the network of inferences, while those readers more versed in mechanics could fail in making the correct analogical inference altogether.

Benyon (2014, pp. 191–196) elaborates a bit further on the topic of metaphors for the design of interactive systems. He strongly advocates that designers cannot avoid metaphors in interaction design, so metaphors must be considered explicitly in the process of design. The author notes how indeed the most relevant feature of a metaphor is to include good conceptual correspondence between two domains (usually a new one and a more familiar one), but also that the metaphor design does not imply a physical resemblance, even though occasionally it is appropriate. The result is that usually the metaphorical representations are blends of characteristics that are recognizable parts of both the domains, which possess their emergent structure. Some examples are the *windows* in desktop computer interfaces, which blend the domain of physical windows for the property of allowing to “look into” something (a file), and computer windows which display information in a confined space. Another example is the *folders*, blending the characteristics of the domain of physical folders in which papers are stored, and the domain of computer files, which have a physical and organized location on disks. The designer conceives this blend of characteristics to describe a new domain to other people, for example a new software, a different layout or interactive services. We can say that this communicative intent exploits the capacity of the designers to make use of the linguistic and semiotic properties of the metaphor as a first, but also the designers have to actively try to control the set of implications arising

from the relation they are proposing between the two domains. This is discussed amply in Chapter 4.3.

The author does not go further in depth in the analysis of the complex inner workings of the conceptualization of a new metaphor. However, he proposes a set of guidelines of practical use while designing a metaphor:

- *Integration*: a metaphor integrates two domains but it also tends to blend their features and characteristics, which need to remain coherent. The metaphor creates its own structure, the relationships between concepts need to be safeguarded.
- *Unpacking*: people should be put in the position to be able to analyze the metaphor, its inputs and their relationships. Interpretation is involved in the process, but the designer can ease it by picking only the relevant information.
- *Topology*: the structure of concepts and their organization should be coherent between the domains that are put into relation. Otherwise, it makes it difficult for the people to navigate the concepts.
- *Analysis*: the designer should explore the metaphor to convey only the appropriate functionalities and concepts.
- *Design*: the designer should choose an appropriate visual representation for concepts, objects, and actions. Of course, the visual representations do not need to be realistic, but only metaphorical.

All these recommendations are taken into consideration in Chapter 5.

Another piece of advice the author proposes which is worth elaborating further is that the designer through the metaphor should aim for people to derive appropriate expectations, which can be seen as related to the *unpacking* guideline. This recommendation resonates with what is discussed in Chapter 4.3.1: metaphors are not a mere transposition of meaning, but they include the sign producers' will to express particular sets of concepts, while they induce the receiver to focus on these salient

features disregarding others. During the dialogue, new meanings are formed and assigned to the relationships between concepts, in an interactive way. The process is not solely in the hands of the sign producer, but it is ultimately driven by their will to communicate something in particular. A meaningful and moving metaphor is *never given nor found*, it is *elaborated* and made explicit in its most needed parts. Choosing a metaphor is a big commitment for the designer because it needs analysis, maintenance and adjustments that are bargained with the users over time.

This concept is supported by Sharp et al. (2019, pp. 439–441), who describe in their view that suitable metaphors and analogies are informed by the designer through immersion in the data and the attempt to understand the users' perspectives, looking for a balance between utility and relevance. The authors (Sharp et al., 2019, pp. 74–79) note how metaphors and analogies suggest to people how to use the interface for an activity or a set of actions (e.g. browsing, bookmarking, searching, revisiting). In turn, the metaphor suggests to the designers how to articulate the relationships between concepts, such as “containment” (e.g. folders, panes etc). Notably, the authors describe how the *search engine* metaphor was defined to befit a software which indexed and retrieved files through an algorithm working in the background and for daily use. The metaphor indeed compares the software to a mechanical engine, which has several parts working jointly ready to support the everyday action of looking in different places to find something. The user does not know exactly how the engine works either, in most cases.

Speaking of the appropriateness of the application of metaphors, Rosenfeld et al. (2015, pp. 367–370) provide an interesting classification of types of metaphors in the design of information environments:

- *Organizational metaphors*: metaphors which leverage the receivers' familiarity with a specific system's organization to quickly introduce a new system's organization. E.g.

speaking of a new online service as if it was a retail market which everybody more or less is expected to know.

- *Functional metaphors*: metaphors which provide organization to tasks performed in known or traditional environments to quickly introduce the receiver to tasks in a new environment. E.g. describing a service which provides indexing, searching and browsing as if it worked like a library.
- *Visual metaphors*: metaphors which leverage the receivers' knowledge of sets of graphic elements to introduce the receiver to new graphic systems.

We can state that the classification is of particular interest because it provides further layers of analysis to the information designer: (1) it supports discerning different kinds of information within the two domains that are put into relation by the metaphor or analogy. Sometimes the domains are so complex that it is difficult to filter relevant information with ease. The categories also provide grouping for the information by some rationale of immediate practical use. (2) Indeed, the typologies of metaphor can lead to a more or less adherent categorization of the information; labelling sets of information iteratively while conceiving a metaphor is as fundamental as not always intuitive. De Souza (2005, p. 81) defines this process of categorization as "grammaticalized metaphors", an organizing principle of the interface language, in which users *expect* the figure of speech to extend to all similar contexts. Categorization and structuring of information lay at the basis of any correlation between terms and groups of terms (as described in Chapter 4.3.2). Any help in this task from design methodology is an asset for the information designer. (3) Different types of categorization can be explored with dedicated methodologies for information structuring and rendered visible to different design artifacts. Flow diagrams or network models can represent organizational metaphors more directly, while Hierarchical Task Analyses can support the representation of functional metaphors. Visual metaphors can be based on a completely custom information

design on their own. This latter layer of analysis might seem the more trivial one, but it is probably the most enabling one for the designer: being knowledgeable and trained to reify various forms of knowledge (especially the new and most complex ones) makes the information designer competent and confident. Conceiving or unpacking metaphors is not a simple task. Being able to rely on models for where to start the job is usually of great practical value.

What is interesting, is that the Machine as a model for a metaphor touches upon all the three types enlisted by Rosenfeld and colleagues: It is a metaphor that (1) organizes space, both through means of conceptual structure and visual layout: the reader perceives to deal with pseudo-physical mechanical gears, and the domain is mechanics so conceptually everything should run according to a plan. At the same time, the information (gear groups) is laid out in a way that organizes the narration of the metabolism pathways. There is a method behind the arrangement of gears and pulleys. (2) It is a metaphor that implies a logical organization of tasks, all belonging to the construction of a pseudo-engine: the various parts have specific mechanical functions (gears, pulleys, differentials, “handles”), and whoever wants to interpret the working of the metaphor had to be at least introduced to the very basics of mechanical operations or to have dismantled a geared engine at least once before. There is a method behind the arrangement of the chain of reactions starting from the bottom left of the machine, understandable by whoever spent some time in a workshop as if they would try to build an actual mechanical model out of the Machine. Those who never observed or repaired anything mechanical will hardly get the functional model embedded in the artifact, as much as whoever never approached a library would understand an online digital catalogue. (3) The Machine is fundamentally a visual metaphor, that renders visible through a custom set of graphic elements a phenomenon that is invisible by nature, and which is usually represented by more abstract means, such as flow

diagram representations. Possibly, this last feature of being a visual metaphor is what necessarily includes the other previous two: the need to represent a phenomenon through the visualization of another domain implies the organization of the internal structure of the graphic elements (otherwise no analogy can be made, extending from the conceptual sub-stratum upward to the surface visual representation). At the same time, making a meaningful visual metaphor also requires a certain degree of knowledge of the organization of tasks performed in both the domains that are put into relation, to know “what I am expecting to do with this information”, to create expectations for clear actions or hypotheses of actions.

4.

Universes behind a Machine: analogy, representation and scientific practice

To provide as in-depth an account as possible of the knowledge domains incorporated in the Machine de Lejeune, the following chapter touches upon the literature from several disciplinary fields related to the theme of analogy, scientific models and visual analogies.

4.1.

Representation as a narrative device for explanation and persuasion

Looking at the domain of images, over the centuries representations have been used not only to clarify or explain some concept but also to interest people in the symbolic content of the image as much as to persuade the spectator to follow the vision embedded in the representation.

Lina Bolzoni (Bolzoni & Mino, 2017) proposes a significant point of view on the role of images through the centuries. She refers primarily to the “symbolic images” the likes of the ones used for preaching purposes, but it is possible to extend

the same reasoning to models which are strongly based on visual representations, such as the Machine. They are indeed all communication artifacts expressly made to stimulate curiosity and to close the gap between the current spectator's knowledge and the complexity of the concepts embedded in the representation itself. To do so, symbolic images made ample use of analogy, metaphor and allegory as a means to narrate and persuade the reader-spectator.

As Bolzoni remarks, these kinds of representations are images that must be read and require time and attention. The reader-spectator is challenged to understand them. The challenge though does not remain always the same, the reader-spectator brings new life into the representation depending on their imagination and fantasy. This is probably more evident in the most ambiguous or voluntarily vague representations, less so for a scientific representation which is supposed to provide precise notions to the reader. However, as it is amply discussed in Chapter 2.4, the choice of the visual analogy is not neutral nor given: it is strongly related to the vision of the scientist of the problem and to the world they live in, and results in implications for its correct reading. The passage of time can lead to the legitimate ignorance of the reader-spectator of the historical and scientific context at the time of the production of the artifact, and as a consequence the meaning that the reader-spectator attributes to the representation might vary. Inevitably, over time the meaning of some features of the image gets lost or even becomes obsolete, but this way they leave room for the image to spark new interest even in different contexts. For example, the Machine is based on the representation of an analogue calculator (the Pascaline) which was century-old obsolete even at the time of the conception of the visual analogy. In the '70s-'80s electronic computers were already advanced. Nowadays the analogy exudes an even more obsolete feeling, since current society is not used anymore to bulky mechanical machinery as it was until the XIX century. Without understanding the reason for

the choice of such old-fashioned representation, the contemporary reader-spectator is free to speculate on the meaning of the representation and even stipulate their own interpretation. Precisely for this phenomenon, the Machine entices the act of approaching its intricate clockwork details to discover the inner workings of such representation.

Bolzoni also illustrates how these sorts of representations live right on the edge between the mental dimension and the representation dimension. Some images correspond to the logic that they want to convey, and therefore they help us envision the delicate interplay between memory, which is deposited in the images, and the invention of those who look at the images and try to understand them. The example she brings up (Bolzoni & Mino, 2017, pp. 18–34) is of great interest: the *Turris sapientiae* (Figure 17). The representation condenses a long tradition of literature within a simple scheme, which is meant to lead the reader to create in their own mind a pathway through moral concepts. At the base of the tower, the foundation columns bear inscriptions of the four cardinal virtues, on top of which bricks and arches are stacked to build up the “moral building”. The entrance door to the tower is accessible through a staircase, which steps are a physically perceptible effort to make to build the person's morals. Some representations become *imagines agentes*, “images which act”, which are capable of striking the imagery of the spectator and which take the appropriate form to act towards the spectator like actors in theatres do. Judging by Lejeune's writings on the Machine, we can observe that his efforts to create the Machine were moved by similar motivation, to narrate through its representation the scientific, ethical and practical visions leading him, in the attempt to strike reasoning and conscience of colleagues and public opinion.

Curiously, what Gabriele Mino describes (Bolzoni & Mino, 2017, pp. 43–44) about representation in alchemy over the centuries applies to some degree. Indeed, up until the XVII–XIV century, alchemy tried to represent chemical processes, although

ignoring the underlying chemistry and mathematical principles and via observation and experience. To express such experience, alchemists made use of a variety of representations, mainly allegorical, coming from the most diverse traditions, including Christian religion or pagan ones. The communicative power of these representations lies in their syncretism, the ability to put together imagery from varied and different avenues of knowledge, due to the lack of more precise description tools. By no coincidence, the use of imagery from different domains is what defines an analogy or a metaphor. Lejeune's Machine can by no means be compared to alchemical representations, the context is completely different. However, the need to express a metabolic problem which is known just in its principles leads Lejeune to resort to a visual representation based on an analogy with mechanics to better scope the problem, at least as a start. The spirit and the intention are similar, leading to a result that is markedly different from the other more common traditional link/diagram representations (as observed in Chapter 1.4).

From these reflections, it can be stated that representations based on analogy or metaphors can be conceived as a dialogical instrument, a characteristic that is desirable in objects of design. Borrowing from Flusser (2003, pp. 51–55), an object of common use is not just an instrument to deal with other objects, but they are *media* (in the sense of mediator instruments) which enable the user to interact with other people. Given this context, these objects carry with them not only their objective reality but also intersubjective interpretations and use, they are not only problematic but also dialogical. The designer who creates the project for the object faces the responsibility (and therefore a problem of freedom) to produce something that does not hamper the others using the object, and to be accountable for it, loyal to the user. By truly considering this responsibility, the designer can enhance the communicative, intersubjective and dialogical aspects of the object over its objective and problematic qualities. This attention towards the other people, the user, is itself a form

of progress, of literally progressing towards the other people. This feeling of responsibility can lead to the design of better objects of common use and technical and scientific advancements if paired with the control of the objective and problematic qualities of the object. Flusser refers mainly to everyday products, with tangible shapes, however by extension the object of common use can be conceived as artifacts meant to be used frequently as a tool, which in the general context of scientific research can be also a model.

As Chapter 2 describes, Lejeune built his model to support his scientific reasoning, but also as a tool to be used to dialogue with the research community in medicine and biochemistry, including and superimposing findings from other research literature, as a map to illustrate hypotheses to colleagues at conferences, as conceptual support to his ethical and political positions. The Machine is a tool which has been permeable to the research community since the beginning. It was not conceived to be a specialized model only for internal laboratory use, but as an instrument to narrate, explain and persuade in varied situations. Lejeune elevates the dialogical dimension of the artifact beyond the limited formal value of the model at the time, for which Lejeune was always transparent, and for which he also wrote a great deal of literature to illustrate and educate the reader. The sense of responsibility he infused in the model of the Machine makes the artifact interesting even nowadays, both in biochemistry and in the design field. Lejeune's intent to progress towards other people through the artifact is explicit, and it becomes part of the communicative power of the artifact itself. The clarity of the intent and the genuine interest to make a visual model that could be used even by others, together with the technical skills to realize it conceptually and practically, is what makes us consider the Machine as an act of design.

4.2.

Usage of representation in scientific and laboratory practice

With the term “laboratory” I describe contexts in which scientific research happens: where discussion among peers sparks from the shared review of data, documents, artifacts, and the debate involves people as much as artifacts in a seemingly infinite spiral of suggestions, clues, stances, pieces of evidence, steps backwards, errors, etc. I do not assign a location meaning to the term laboratory, since it can also be an imaginary (yet experientially tangible) space generated by a discussion over the phone or internet. However, in biochemistry often the discussion space and the physical space are shared, due to the physical equipment which the researcher needs to have access to.

The usage of visual artifacts is of undoubtful importance in laboratory practice, and for communication design the discussion on how representation is used in scientific practice becomes a core topic. A particularly relevant discussion is brought up by two edited books (Coopmans et al., 2014; Lynch & Woolgar, 1990). The papers and the commentaries collected in these books are by sociologists, anthropologists and philosophers, focusing on what happens in the laboratory when scientists interact with representations of various kinds. What emerges is that the overall context of the debate in the laboratory influences which features of these representations become relevant.

Vertesi (2014) discusses a basic concept about the usage of visual representation in a laboratory environment: producing and manipulating visual artifacts is a way “to see new things”, to make hidden features “pop out”, to discriminate between different units. This operation is not made for producing ambiguous images to interpret but to act upon these images with skilled eyes and hands working in concert. The author here discusses image manipulation (more specifically, the manipulation of

colours made by NASA scientists on pictures of Mars's surface), which operates differently than creating a visual analogy from scratch like Lejeune did with the Machine: the former is a way to enhance and interrogate a visual artifact that has been collected through a photographic medium that refers to a tangible reality, the latter is a drawn scheme of an abstract conceptualization of invisible referents. The phenomenology is different, but none of them is more or less “convincing” (Latour, 1990). Both of them are technically produced to highlight some features of the referent and overlook all the others. Their function is to allow for discussion and investigation within the laboratory personnel first, and then hopefully allow the spreading of the researchers' inferences throughout the whole scientific community (Latour, 1990). Indeed, Lejeune (1980) himself highlights that “the true machinery is much more sophisticated than this primitive oversimplification [...] Nevertheless the analogy can be of some heuristic use. As BERGSON once stated ‘we can really comprehend a thing only if we can propose a mechanical model of it’”.

Vertesi (2014) also focuses on the fact that scientists while working with purposefully targeted visual constructions blur the boundaries between epistemology and ontology, as much as making drawings and seeing are not easily distinguishable anymore. Images in science are produced (firstly conceptually and then technically) to draw a natural object as an analytical object. The author cites the historical example of Galileo's drawings of the moon in *Sidereus Nuncius*: he produced such visual artifact not only because he had the skills and the technology to do so, but because his purpose was to draw the moon as a topographical body in a Copernican sense, with all its imperfections and earthly appearance (Winkler & Van Helden, 1992). Thus, Galileo opposed the Ptolemaic stance of heavenly supernatural celestial bodies. Galileo did not draw just what he saw in his telescope, but he embedded his theoretical views in his representations. Moreover, Vertesi (2014) discusses that the skill of Galileo

to make such depictions of the moon surface enabled Galileo's knowledge (and vision of the world) to travel and be reproduced.

I argue that this attitude towards a representation is similar to the one that animated Lejeune in composing his Machine: Lejeune (1980) argued that medicine should be a "third way", between the screening and selective abortion of fetus diagnosed with Trisomy 21 and the lifelong therapy and management of the symptoms caused by it. He strongly advocated for a precise way of acting towards the medical treatment of the genetic condition. Perhaps this was one of his reasons to produce a visual representation of a "broken machinery that we as physicians are ethically compelled to fix". Perhaps the analogy happened by chance, or perhaps he was technically prepared to make it, nevertheless the visual analogy contributed to making his vision of the world become an *immutable mobile* (Latour, 1990), an artifact that can be shared among the scientific community and hopefully gain influence and consent. Galileo's drawings influenced future viewings, depictions, and theoretical understandings of the moon (Vertesi, 2014). Lejeune approached the representation of the Machine with a similar spirit, regardless of the more modest diffusion of his representation.

Continuing over this topic, but taking a little step back over Lejeune's definition of the Machine as a "primitive oversimplification", it emerges the question: is still this analogy between biology and mechanics trustworthy enough to gain biochemists' interest and becoming of some heuristic value? The answer lies in the extent to which the relationships between the domain of mechanics and the domain of molecular biology are respected and effectively represented. This issue pertains to the mathematical model that the two domains are supposed to share, by means of proportions at least. I will not go in-depth in this part since so far I don't have data to support any claim about any formal relationship yet. However, I would like to discuss the trustworthiness that a representation such as the Machine del Lejeune might inspire to specialist readers like biochemistry

researchers. The artifact surely shows face value: I have already shown that Caracausi et al. (2018) made use of parts of the Machine as a heuristic tool in publishing research about the metabolism of children with Down's Syndrome. The group at the Laboratory of Genomics is involved in Lejeune's vision, and by no chance a representation made by Lejeune gains importance given the legacy the laboratory carries forward. This feature was enough for them to use such an artifact as a map for quantitative enquiries.

Amann & Knorr Cetina (1990) provide a sociological point of view on how the materials in the laboratory are visually inspected and how then the scientists make sense of the data conveyed by those materials. They also make these observations by discussing the work in a molecular genetics laboratory, even though they discuss a particular type of visual artifact, namely the autoradiograph of DNA or RNA. fragments, which is completely different from what the Machine de Lejeune shows. The authors argue that there are at least three different modes of practice through which materials in the laboratory are visually inspected:

1. *manual and instrumental enhancement*: improving the visibility of observable materials. For example, holding a test tube against the light to assess the progress of a biochemical reaction;
2. *inspection of the "data"*: to inspect the results of the test taken. For example, checking the segments of D.N.A. or R.N.A. on the film;
3. *preparation of the "evidence" for publication*: a process of selection and transformation of the information makes it suitable for being presented.

The first phase usually does not spark too much discussion, because it is taken care of by shared laboratory procedures normally. The second phase, the discussion of data, is the centre of the scientists' attention. In the third phase, scientists select and transform data to make it suitable to be published. Lejeune's

publications provide an ample variety of accounts of visual and scientific materials, which are useful to envision some examples of the above-mentioned kinds of materials.

In the article from Lejeune & Turpin (1962) it is possible to see a clear example of the second kind of material, a notable one as well. In the article, Lejeune synthesizes the evidence which led him and his colleagues to isolate the cause of Down's Syndrome, i.e. the supernumerary chromosome 21. After isolating chromosomes from a cell of a normotypical female subject, by rearranging the full set of 46 chromosomes (**Figure 18 - Plate IV.1**) and examining their arrangement (**Figure 18 - Plate IV.2**) seven groups of chromosomes emerge. In the bottom row, it is possible to note that the Y chromosome is absent (while an X chromosome is present in the last pair in the third row from the top), with a pair of Vh and a pair of Vs chromosomes. On the other hand, the cell of a male subject with Down's Syndrome showcases a full set of 47 chromosomes (**Figure 19 - Plate IV.3**). In the bottom row of the karyotype (**Figure 19 - Plate IV.4**), it is possible to see that there is a supernumerary Vh chromosome (with the Y chromosome normal, while absent for females). These very early accounts of abnormalities in the karyotype were confirmed by other scientists across the world in the early years of cytogenetics, in the late '50s and early '60s. From these findings, Lejeune and colleagues hypothesized that a plausible explanation for the anomaly is the occurrence of a non-disjunction process during meiosis. A process they observed some years earlier also in the chromosomes of fruit flies. Not by chance, the anomaly happens also more frequently with the ageing of the fly, paralleling what human data also illustrate.

It is interesting to see how the explanation of an abnormality is rendered evident through the illustration and discussion of materials used for the inspection of the experimental data. These materials and evidence led to the discovery of the causes and fundamental etiology of Trisomy 21. Images which made the history of genetics.

Figure 18

Visualization of chromosomes and karyotype of a normotypical girl.
Retrieved from Lejeune & Turpin (1962): Plate IV.1. - Microscopic view of the 46 chromosomes of a normal girl; Plate IV.2. - Karyotype of Plate IV.1; 22 autosomic pairs of chromosomes + 2 X chromosomes.

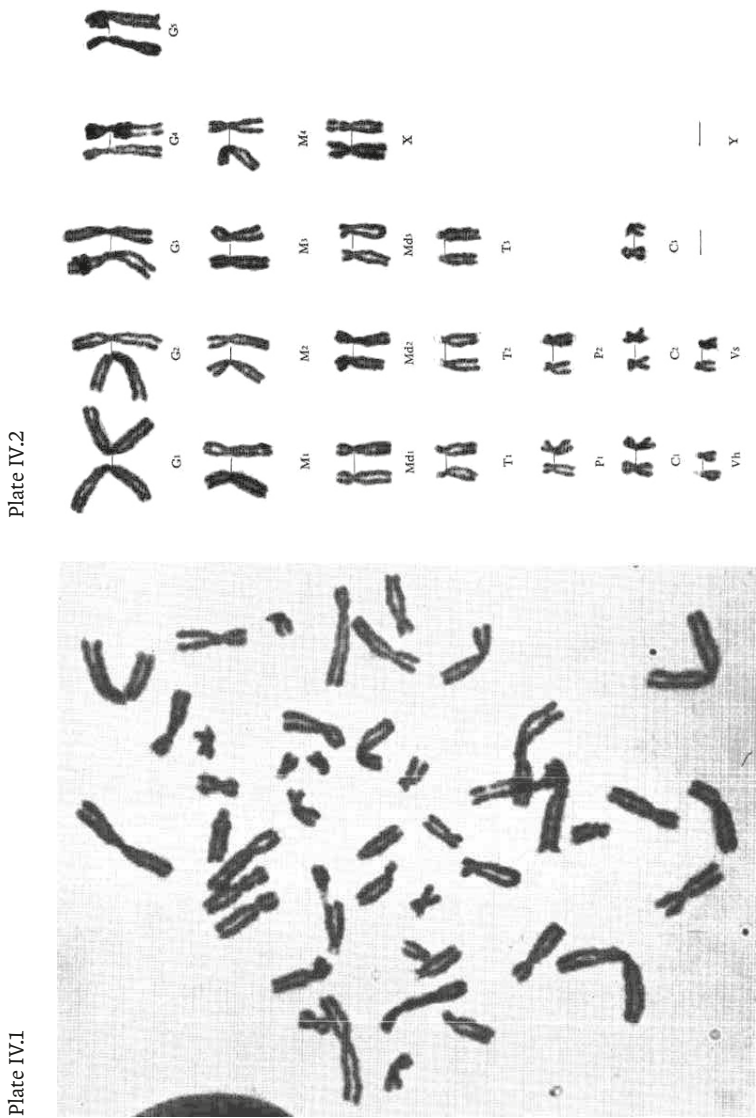


Figure 19

Visualization of chromosomes and karyotype of a boy with Trisomy 21.
Retrieved from Lejeune & Turpin (1962): Plate IV.3. - Characteristics of chromosomes in a boy with mongolism; 47 chromosomes; Plate IV.4. - Karyotype of Plate IV.3; 22 normal autosome pairs + 1 X chromosome and 1 Y chromosome. Note the extra chromosome (arrow) of the Vh type.



Plate IV.4

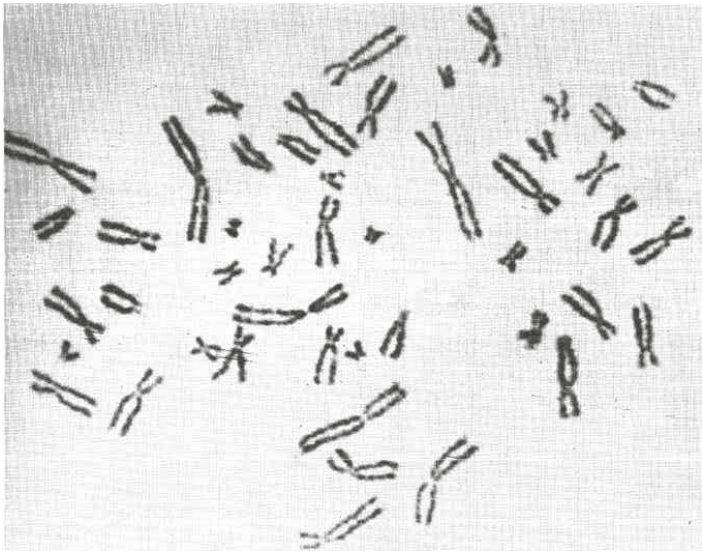


Plate IV.3

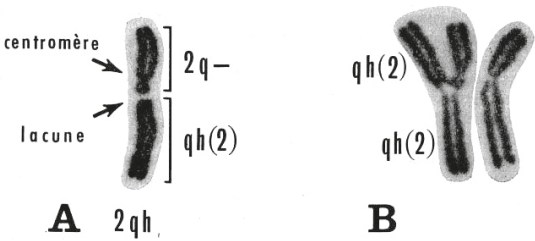
A small but curious example of “preparation of the evidence for publication”, which is still related to the use of the karyotype visualization for expressing hypotheses and evidence, is provided by Lejeune et al. (1968). In the article, Lejeune and colleagues literally *scope in* to a very specific chromosome (chromosome 2, in the karyotype the second from the top going to the right) to illustrate an abnormality in the long arm of chromosome 2 found in the karyotype of a woman and in one of her two daughters. The woman suffered from markedly deficient intellectual development. Without going too much into the scientific hypotheses sparking from the observations, what is interesting for this discussion is how the authors prepared the picture of the gene for the publication (**Figure 20**). The representation of the chromosomes (abnormal and normal) is used as a “living” reference frame, which is enhanced by notation that provides context and explanation to support the discussion. Some knowledge of genetics is required to read the scheme correctly, but with the help of the caption the phenomenon is unfolded and embedded conceptually in the same tangible matter that originated it. Graphical mediation between the representation and the explanation is present but in a very basic manner. No further schemes or diagrams are provided, the morphology of the chromosomes is exposed as-is and only enhanced by the typographical elements.

An analogous use of image and notation is visible in **Figure 21**, a plate from Turpin & Lejeune (1969, pp. 31–32). In the representation, the authors visualize the classification of chromosomes depending on the positioning of the centromere. This classification is one part of the two conventions which allow the researcher to arrange and number the chromosomes in a standard layout (the karyotype), the other convention concerns the relative length of the chromosome. Again, the chromosomes are used as embodied reference frames for the surrounding information, and their shape is part of the writing system as much as the surrounding alphabetic text and arrow notation.

Figure 20

Details of abnormal and normal chromosomes with notation.

Retrieved from Lejeune et al. (1968) Fig. 1.

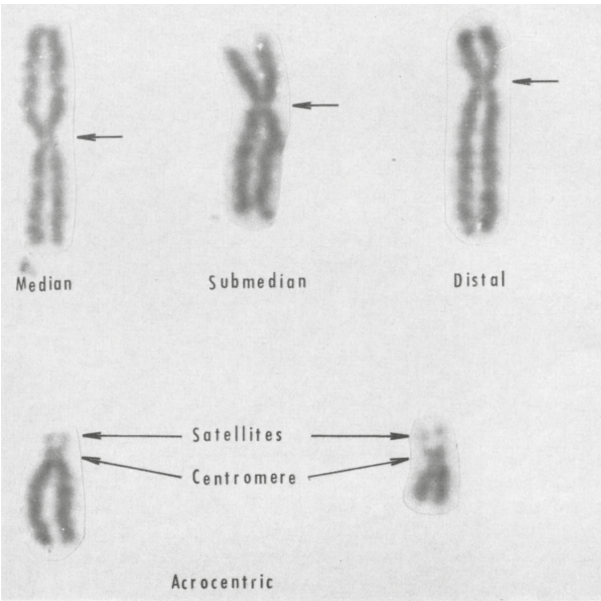


Note. A: The abnormal chromosome 2, 2 qh, has a gap at some distance from the centromere, on the long arm; B: In an otherwise completely normal mitosis, one of the chromosomes of pair 2 (the only one shown here) has undergone selective endoreduplication of fragment qh (2), whereas fragment 2 q- is normal.

Figure 21

Classification of the positioning of chromosome centromeres.

Retrieved from Turpin & Lejeune (1969, p. 32).



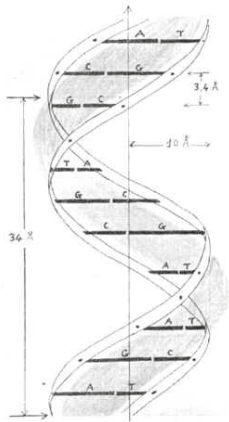
Another article from Lejeune (1958) is a particularly interesting example of a publication where the scientist makes use of different types of representations to explain a topic while also making an argument utilizing the visual and material models represented. To explain the nature and the mechanism of DNA and its duplication, Lejeune starts by borrowing the double-helix model directly from James Watson and Francis Crick (**Figure 22**). The model synthesizes visually the most salient features of the Deoxyribonucleic Acid (DNA): the two helical backbones composed of pentose deoxyribose and phosphoric acid, holding together the chains of Purine bases (Adenine and Guanine) and Pyrimidine bases (Cytosine and Thymine) to form a nucleotide chain. What the model highlights is that the only way to form hydrogen bonds between purine and pyrimidine bases while maintaining the width of the overall fibre is to make precise pairs (Adenine with Thymine and Guanine with Cytosine, **Figure 23**) in a dextrorotatory spiral. Due to the invariance of arrangements between bases, given one chain of bases its complementary one is always determined. It is therefore possible to envision the mechanism of DNA duplication, using a material model which Lejeune attributes to his colleague Dr. Jean de Grouchy (**Figure 24**): (1) if the chain is open, with hydrogen bridges open at one end, (2) the fragments of bases and deoxyribose scattered in the cell nucleus can attach to complete the open fragment. Only the appropriate pairs form, the others are discarded. (3) Repeating this process contributes to separating the original molecule into two complementary chains sharing the same arrangement. The result is two new DNA molecules that are identical to the original molecule.

In the article, Lejeune makes use of three different kinds of representation with a significant ease in the transition. Each figure serves a specific purpose, and the technique of representation is not only the available one, but the appropriate one to convey the most fundamental meaning.

Figure 22

Model from Watson and Crick synthesizing the structure of DNA.

Retrieved from Lejeune (1958, Figure 4).



Note. The representation shows two lateral ribbons made of chains of phosphate groups and pentose deoxyribose sugars, attached to nitrogenous bases (A, G, C, T) molecules seen from the edge.

Figure 23

Representation of hydrogen bonding between bases.

Retrieved from Lejeune (1958, Figure 5).

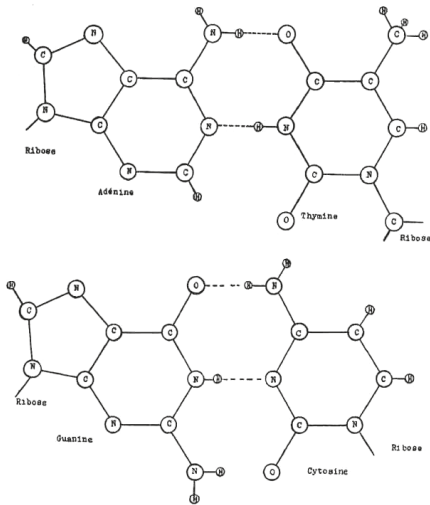
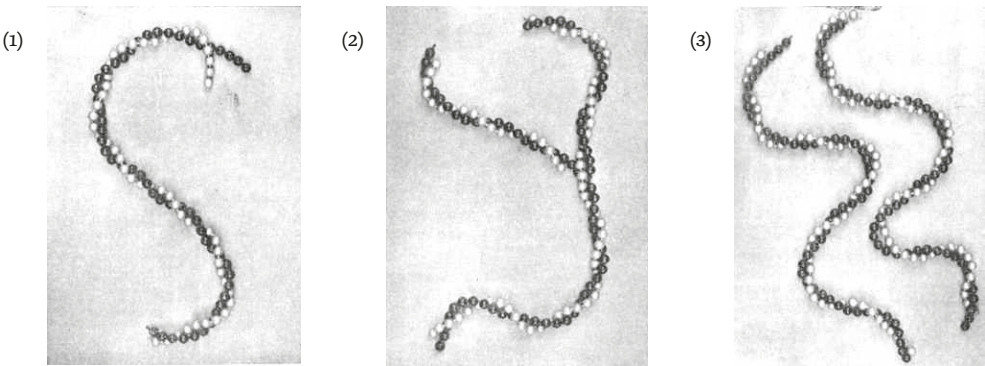


Figure 24

Material model showcasing the basic mechanism of DNA duplication.

Retrieved from Lejeune (1958, Figures 6 to 8).



The scientist straddles between giving a precise enough account of the scientific knowledge acquired by the research community up to that point and simplifying the communicative message enough to render it understandable to most readers. These varied but coherent materials highlight how visual representation is a means to communicate and to provide a basis for discussion, to support the scientific discourse and to contribute to its popularization and dissemination as well.

As Amann & Knorr Cetina (1990) state, “data act as a basis for sequences of practice rather than observation at a glance”: in the situation, the scientists are attracted, gather, inspect and handle the materials, while discussing verbally. The perceptual identification of data is achieved not just by language description, but through conversation. Quoting the authors, “the process is not just a semiotic process, in the sense of involving a translation into a generalized system of signs. Nor is it mainly a cognitive or interpretative process in the sense of involving individual conceptual decoding. Instead, the process has a speech act and particularly a dialogical or interactive structure”. While conversing, the scientists do not follow a strict sequence of questions and arguments (even if it is somewhat possible to discern general categories) but they sidetrack using conversational devices of various sorts. One of these devices is described by the authors as “optical induction”, a sort of hybrid between visual operations and conversations. This process is non-linear, and it is stimulated by the visual features of the materials under investigation: the scientists interrogate themselves about the image, which variables might explain the visual behaviour, explore the geography and the architecture of the image, there is a “here” and a “there”, there is a space in which getting lost and in which follow each other.

All in all, we can say that the visual representation creates a conceptual space in which the scientists can immerse and enact their considerations. This concept is well discussed also by Prentice (2014), who describes how orthopaedic surgeons

definitely inhabit the patients' bodies while looking at the video feed coming from a probe inserted into the patient's articulation. The surgeons then discuss as if they are literally navigating the patient's body while moving around the apparatus, which becomes a sort of technological extension of their body (eyes and fingers first). The image stream enables them not only to factually envision the domain but also provides a shared ground for discussion among specialists and with non-specialists too. The particular feature of this last example is that the relatively large dimension of the elements to investigate (joints) allows the scientists to “shrink” down their perspective and to imagine witnessing in first person the phenomena. Moreover, they can also touch the patients' joints from outside, fostering proprioceptive information. The domain of the Machine de Lejeune is sensibly different: even if today's technology produces graphical simulations of genes, proteins, enzymes etc, the domain of microbiology is pretty much invisible. There is no enhancement of images that can happen like for the pictures of the surface of Mars or the joints of a person. Microbiologists collect data directly from biological samples. The reality, the factual domain, is invisible and it is treated as an abstract domain. Hence, there is a need for visual schemes to envision it.

The Machine de Lejeune creates a space for the discussion of something otherwise difficult to act upon. And it fits with the practice of discussion that happens in the laboratory (Amann & Knorr Cetina, 1990):

- it does not fit with the practice of (1) “manual and instrumental enhancement”, given that it is an analogical representation of the domain;
- It fits with the (2) “inspection of the data” practice, allowing for mapping, exploring and discussing the data. This already happened in Caracausi et al. (2018), but also during my meetings with Prof. Strippoli, in which we wrapped our heads over the gears of the Machine for hours;

- It is possible that the Machine does not fit well with the (3) “preparation of the evidence for publication” because the model might not be exhaustive enough or because it appears strongly different from the current schematic standards.

What emerges from the literature around representation in scientific practice, is that the situation in the laboratory determines which features of the visual artifact become relevant for the discussion of the data. To me, it is evident that the Machine is certainly a very simple model, but it has the power to create the space for an *embodied* experience. There could be a perceptual/psychological but also an epistemological and ontological advantage in using a digital but skeuomorphic system like the digital Machine in the field of biochemistry. I argue that the Machine the Lejeune shows face value at least as a heuristic and conversational tool for laboratory work. It could be that the Machine, which allows for the manipulation and the exploration of a conceptual but tangible environment, reduces the threshold of access to information in comparison to a system of abstract conceptual relationships (like KEGG Pathway maps, see Chapter 1.4), assuming that both forms are mathematically linked to the underlying biochemistry in a correct way.

4.3.

Metaphor, analogy and analogical reasoning

All the considerations about the sociology of the context of use of visual artifacts in scientific practice intertwine with the fact that the Machine represents an analogy between the metabolism of nervous cells and an analogue calculator. This brings a whole background of cognitive sciences and philosophy of science debates over the usefulness but also the slipperiness of analogy in scientific reasoning. While using visual artifacts

for scientific purposes, or even for learning, the context of use involves several layers of complexity simultaneously:

1. There are the language skills of the reader, which must interact with the properties of language implied by analogical transfer of meaning;
2. There is a visual representation, which is not objective about the factual reality, it is already encoded in some way, from which derives some kind of meaning;
3. There is a phenomenology of perception of the reader, what his/her senses pick up from the scene;
4. There is the reader's subjectivity, namely their cognitive ability, background, training, etc, which supervises and interacts with all the other layers.

Moreover, given the analogical and mechanical nature of the Machine, the artifact suggests (*affords*) conceptual restrictions over its inner workings. The Machine represents an invisible domain, the biological one, that is investigated by means of data analysis in everyday practice. For the readers of the Machine, the way the restrictions of an invisible domain apply to something conceptually tangible as a mechanical calculator is a matter of making the correct inferences. This means for the readers to follow and control the opportunities generated by the metaphor and the analogy embedded in the visual artifact.

The goal of this chapter is to provide descriptive tools of metaphors, analogies, and models for the conscious use of these linguistic, rhetorical, and thinking devices also in the design of visual communication artifacts. These thinking devices aim to clarify the inherent complexity of phenomena that can be observed or hypothesized and thus are a tool for the accessibility of information, a field of research that is proper for information design. It is no coincidence that the main knowledge inputs of the chapter come from semiotics and philosophy of science literature, as fields of knowledge that deal with meaning, logic and the communicative sign. The intent is not to provide a cohesive theory of the usage of metaphor, analogy and models for visual

communication design and neither is to produce theories to be applied directly deductively by designers, but to collect epistemological inputs for the visual communication design field from those disciplines involved in the study of language, logic and education. The inputs are made available to the designer, with timely examples on the Machine artifact, to create methodological insights into these complex and not easily controlled rhetorical devices for the design of visual artifacts.

To get a good foundation for the discourse, it is important to define and confine as best as possible the meaning of *metaphor*, *analogy* and *model*, since these terms can overlap to some extent, but mostly because they have been used alternatively by different disciplines. Some framing of the terms and their implication for this dissertation is needed.

In his extensive dissertation on metaphors and analogies for didactical use in mathematics, Salvi (2014) collects a significant amount of literature and a number of models on the topic. Even though the intent behind the Machine representation is not didactic, not even explanatory, but heuristic and communicative, the insights brought up by the author are of noticeable interest for the design of visual artifacts, many of which are of great practical use for designers and educators, starting from useful definitions. He highlights how currently a clear distinction between analogy and metaphor is not shared yet. There is still much controversy on the topic despite the great interest in analogue reasoning in fields like Cognitive Sciences and Artificial Intelligence. However, there is a general agreement in literature on the fact that there is a strong interplay between these two concepts and also with scientific models (see for example Black, 1992; Hesse, 1980). Salvi (2014, pp. 41–49) provides a sound rationale based on literature in philosophy of science and didactics for the definition of the locutions, which is also of practical use for this dissertation. The main points are as follows.

A *domain* (of knowledge) is a set of real or ideal (conceptual) situations which are defined by objects or subjects, actions, concepts, relationships and operations together with a community of individuals for whom such situations have a shared meaning. A *problem* belongs to a specific domain when the elements which define the situation belong also to that specific domain. Two *domains are different* when there is no community of individuals able to identify at least one situation or problem involving elements of both domains and only of these (therefore excluding elements of other domains), and the community agrees on this fact.

An *analogy* is the act of detecting two domains of knowledge (which can coincide), at least two elements (one for each domain) and at least one relation between some of the elements of each domain. Given these elements, the analogy consists of determining a mapping between some elements (at least two) of one domain and the elements of the other, and a mapping between some of the relations (at least one) of one domain and those of the other.

A *metaphor* is any expression that can be communicated to other subjects, in any form (verbal, written, gestural, graphic-pictorial in two-dimensional or three-dimensional form, animation) or any object that allows, in a given context and with objective data, a subject to identify or build an analogy between two different domains.

The term *model* can have significantly different meanings depending on the context and domain. In the interest of this dissertation, for what concerns the domain of science, it can be considered a scientific logical tool of description, explanation or prediction of phenomena, which can be more or less formal, but not necessarily only mathematical. For what concerns more the (visual) representation of knowledge, a model can be considered as a *conceptual model*, which makes perceptible (visible) some terms of an underlying model but which cannot provide

justification as theory due to its intrinsic limitations. These concepts are explained more in detail in Chapter 4.3.3.

It is possible then to trace a quick distinction between metaphor and analogy: the *metaphor mainly concerns the plane of expression and communication*, starting from which analogies can be built. The metaphor can take different forms, oral, written, auditory etc. and it is intended to elicit in the audience the cognitive act of first connecting two domains. However, this creative aspect is not exclusive to metaphor, also analogies can bring the audience to connect two domains. This creative feature of metaphors lets us conceive these logical devices not only as mediators of communication but also as devices capable of aiding the audience in the creation of new knowledge. On the other hand, the *analogy concerns more the conceptual organization and the inferences* that the audience can make after identifying the connection between different domains or within a single domain. In particular, the more complex kinds of analogy involve relations of proportions between elements of the domains. When a model is created or understood via a set of analogies, we can consider the metaphor as its “communicative shell”, which gives way to the complex of implications and attributions between the two domains, that is the analogy.

Salvi (2014, p. 49) then summarizes the path connecting metaphors, analogies and models: from the initial metaphor that ignites the connection between two domains, analogies are formed from within the metaphor on the basis of isomorphisms. The analogies can reveal a model or contribute to creating or understanding a better one. The path can be summarized as metaphor → analogy → model, even though the process is not so linear, but it proves useful to organize the following chapters cohesively.

Here it follows also a specification of terms which pertain to the visual communication design field and that are fundamental for this dissertation.

- *Communication artifact*: any object which embodies or serves communicative purposes (Anceschi, 1988).
- Whichever graphic sign is shown by and on an artifact is an act of *writing* (Lussu, 2003, pp. 11–37), while the deliberate and conscious disposition of elements of writing in the space is defined as *synsemia* (Perondi & Romei, 2010a, 2010b).
- The subjects involved in an act of active observation and understanding of an artifact are therefore *readers* (as also Perondi, 2012 implicitly does). They are defined as *users* when they are involved in the interaction with an interface (no matter if digital or analogue).

Following these definitions, we can state that the Machine de Lejeune is a communication artifact that through synsemia represents cellular metabolism by means of a generative metaphor, “*as if it was a mechanical calculator*”. This metaphor should interest the medical-biochemical researchers (the readers) to investigate the analogies connecting the domains of biochemistry and mechanics.

The next chapter provides literature accounts on the communicative level of the relation between two domains, the metaphor.

4.3.1. Metaphor

Metaphors can support a variety of functions in communication: they can be used to provide meaning to some obscure concepts, to argue or to demonstrate (through analogical reasoning), to analyze a situation (or facilitate the analysis of it) or they can be used to represent elements of knowledge or to communicate them. Being aware of the function the metaphor is supposed to play in communication is of fundamental importance because the effectiveness of the metaphor is in relation to the objective of its conception and situated use in the context.

In any case, the appropriateness of the objective of the metaphor, and the generation of meaningful analogies from it, does not prevent the creation of misconceptions in the reader, which can hamper their immediate and future learning of the elements of knowledge. From these general considerations, it follows that the effectiveness of metaphors and analogies cannot be evaluated *a priori*, since it strongly depends on the plan for their usage and their use in the context, but the characteristics embedded in the metaphor make it possible to hypothesize possible communicative outcomes that can be empirically tested with appropriate scientific methodology. This careful planning becomes even more delicate when the intent of the metaphor is didactic, not just communicative. Salvi (2014, pp. 24–35) reports indeed how authors (Vosniadou, 1989) of experiments on analogies describe how both children and adults showed difficulties in retrieving (accessing) information that they could exploit in analogies to solve new problems, due possibly to their insufficiently abstract representation of problems or the lack of sufficient background knowledge. The representation of knowledge may or may not facilitate the recognition of similarities that can activate an analogy.

In this sense, it is fruitful to assimilate the role of the teacher/educator to the designer, whenever they both face the intellectual and practical challenge of preparing meaningful metaphors and analogies to communicate some message to their readers/users. This presumes to always keep in mind the sensitively different endeavours the educator and the designer are pursuing and the different contexts in which communication happens. For the sake of simplicity, the following paragraphs will use the locution “the sign producer” (Eco, 1976, p. 188) to encompass both the figure of the teacher/educator and the designer, to put the accent on the common goal of producing an artifact made of signs, despite the different objectives of their profession.

Indeed, the challenge of determining a promising metaphor or analogy is similar to the problems which Eco (1976, pp.

187–189) describes for dealing with *content-nebulas* which cannot be analyzed into recognizable and definable content units, yet. This occurs when a discourse happens to not have satisfactory interpretants yet, due to the fact that the verbal expression is insufficient to interpret the whole breadth of contents to communicate. The content (in its nebula-like structure) is not yet coded nor divided into precise units. For a culture to be able to develop an appropriate expression-system to convey the corresponding contents, a highly differentiated content-system has to evolve. A paradox happens, then: the expression system must be established according to a content model which does not yet exist until it is expressed in some way. The lack of a clearly defined content type makes it impossible to find an appropriate expression type, while the lack of an appropriate expression device makes the content vague and inarticulable. The result is that the sign producer has a fairly clear idea of what to say, but they do not know how to say it precisely, and they cannot know how to say it until they discover precisely what to say. To get out of this impasse, the sign producer then must predispose a new sign-function, based on a new way of coding. To propose a new way of coding means to be able to make correlations, which usually are based on conventions which do not exist in this case, generating the very problem. To make the new correlation acceptable, the producer must base it on some evident motivation, a stimulus. If the expression which acts as a stimulus achieves to direct the attention toward certain items of the content, a correlation is posited and it might even become a proper convention one day. Having then rendered the content type recognizable to some extent, its pertinent features can be projected into a given expression continuum through some transformational rules. The more the content-type is new and uncoded, or it is the result of unprecedented acts of mentioning, the more the sign producer must elicit in the receiver some perceptual reactions that are to some extent equivalent to the ones he might have in the presence of the actual object or event.

Eco picks up later (Eco, 1984, pp. 195–198) this concept of universes and nebulas of contents, including it in a more structured view of the function of metaphors. Even though there is no rulebook or algorithm to generate metaphors (especially good ones), it can be observed that the success of a metaphor is the product of the socio-cultural format of its encyclopedia of interpretants: the richer the cultural fabric of the society, the more the universe of contents has the chance to be already organized in networks of interpretants which can discern semiotically the similarity and dissimilarity of the properties to describe. In turn, this universe of contents, which is not strictly hierarchical, draws from metaphors and their interpretation the opportunity to restructure itself into new nodes of similarity and dissimilarity. Within this endless loop of semiosis, it happens that new *tropes* (new metaphors in this case) are uttered, which have never been heard or experienced as if they had never been heard before. Nevertheless, these early tropes can arise because there is already an underlying semiotic fabric, they cannot be born out of thin air. New metaphors use parts of former ones. Eco highlights that to better understand metaphors it is not necessary to know the encyclopedia they encompass because the metaphor is the tool to better understand the encyclopedia itself. This is the knowledge that the process of metaphor production provides, for as complex and not linear as it is: to provide a glimpse into the code of communication of the society and to entice its exploration. Simpler and more confined definitions of metaphor fail to describe such a process, and they are the mirror of the fact that we perceive metaphors as simple when they are definitely not. Metaphors are a mode of expression, and the most interesting ones have (additive) cognitive value, they are not mere (substitutive) rhetorical ornaments. Aristotle described that the metaphor teaches what to look for to find similarities and differences in cultural units, it is a cognitive instrument. The process performed by the reader while exploring metaphors involving

domains that are either distant or superficially not resembling each other is similar to the process of learning something new.

Whenever a metaphor becomes customary, catachresis happens (Eco, 1976, p. 109): two sememes acquire the same corresponding lexeme, meaning that two content units with some common property accept the same expression. Not coincidentally, this process of creative definition of a new code of interpretation parallels that of abduction logic (Eco, 1976, pp. 132–133). The inferential logic of the abduction lives in acts of interpretation of uncoded contexts and circumstances, and it represents the first step of a metalinguistic operation destined to enrich a code, a very evident instance of the production of a sign function. When an ambiguous uncoded context is consistently interpreted, and this interpretation is accepted by a community, it gives life to a new convention and therefore to a coding correlation. The context, step by step, crystallizes into a new and accepted ready-made sentence, as it happens for metaphors which at first need to be abductionally interpreted and afterwards they gradually become a catachresis.

The kind of metaphors which show more the potential to entice exploration of the universe of contents (Eco, 1984, pp. 154–155) are the ones following a proportional scheme ($A:B=C:D$, the fourth kind of Aristotelian metaphors). This scheme is also discussed for the analogy in Chapter 4.3.2. This kind of framework for the relation of the sememes defines a propositional function which is “infinitely fillable”. The proportion can even lack one of the terms (which remains unknown, implied or even forgotten in time) and it still works, which is the case of catachresis ($A:B=C:x$). Eco brings up the examples of the “leg of a table”, in which the *leg* stands to the *body* as an unnamed object stands to the table, or the “neck of a bottle”, following the same principle. The two catachresis are conceived in the same way, but they presuppose different kinds of relations between domains (*functional* properties for the table-leg and *morphological* properties for the bottle-neck), which suggest

different universes of contents to interpret while analyzing the two metaphors.

Abduction and the use of metaphors are concrete acts of interpretation which produce sense beyond the currently known code, in an unforeseeable way. This is part of the flexibility and creativity of language, which can produce new portions of the code (Eco, 1976, pp. 132–133).

Conceiving language as a flexible tool to describe experience and reality resonates with Black (1962, p. 16; 1982, p. 28), for whom the rules and logic of language are not identical to those of reality, but they are speculative instruments to be sharpened, improved, and discarded the moment they have exhausted their function, basing on convenience and utility. Language must conform to the discovered regularities and irregularities of experience, and it suffices that it is suitable to express everything as *it is* or as *it could be*. Less, and the language would not be able to articulate, and more is impossible. Although it encompasses a variety of creative situations, we can argue that this abductive and flexible use of language to deal with content-nebulas can be related to the process in which the sign producer (the scientist, the designer, the teacher, etc) elaborates a metaphor or an analogy. The rhetorical devices “invade” the mental and conceptual modelling first, and then the communication process afterwards, especially in those thought articulations for which the producer lacks precise ways to either express exhaustively the whole jumble of contents at hand, or the current way to express the problem fail to articulate deeply enough novel inferences using the usual encodings.

Not accidentally, a visual artifact (an iconic sign) such as the Machine finds its place exactly in this field of content-nebulas looking for appropriate or better expression systems, which in turn mould the contents to support the expression system itself. The basic elements of knowledge rendered by the Machine, i.e. the metabolites quantities, are known information usually represented (encoded) as numerical entities or as nodes in a link/

flow diagram. When Lejeune challenged himself to find a way to communicate a new important pertinent feature of the content, i.e. the concept of “imbalance between quantities”, the usual encoding by link/flow diagrams was not supporting the communication enough anymore. The analogy with a pseudo-pascalian machine imported via analogy the expression device of the simple arithmetic logic, represented (afforded) by the geometric invariance of mechanical gears. The visual analogy allowed for this pertinent feature on the plane of expression to become perceptible and motivated. The Machine might be a complex example of this process, but even with more simple and punctual analogies, the sign producer surely performs this cognitive back and forth between the need to organize contents in manageable content units and developing an appropriate set of expressions to describe those contents. Language and visual representations provide jointly qualitative and quantitative expression devices to overcome the lack of appropriate pre-existing encodings.

The functioning of models and metaphors is fundamentally the same (Black, 1962, pp. 239–240), their objective is to perform an analogical transfer of a vocabulary in search for new connections between well-organized cognitive fields and to dominate the system of concepts to describe new applications by analogical extension. The thought process is unpredictable in its outcomes, but it is its flexibility that makes it useful in science: the scientist stretches the language by which the model is described to fit rationally the new domain, hoping for the existence of a common structure in both fields. If it does exist, the scientist has an objective ground for the analogical transfer, to investigate the isomorphism of the model and its domain of application. The validity of the model then can be assessed by the extent of its isomorphism with its intended application.

A visual representation including metaphors or analogies makes no exception to the reflections above, it does not escape this logical process nor the use of language. A representation is indeed a communicative sign, and part of language as a

specific mode of expression. By no coincidence, the Machine de Lejeune is conceived as a heuristic tool to support a hypothesis. A hypothesis which was first put together by Lejeune inductively from evidence in literature, but which still lacks a general model that posits a rule, a theory. The artifact articulates a vision and a description of a biochemical reality, but by no means the artifact exhaustively describes it.

In his important work on metaphors and models, Max Black goes very much in depth into the philosophical and linguistic function of the metaphor, revealing mechanisms of great importance to know whenever producing or receiving a metaphor. Black (1962, pp. 27–30; 1982, pp. 44–48) describes how in practice a metaphor is normally found in a sentence or another expression in which some words are used metaphorically while the remainder is used non-metaphorically, and the metaphor does not make up the entire sentence (which would result in a riddle or an allegory of sorts). The expressions used metaphorically become the *focus* of the metaphor, while the remaining parts of the sentence are the *frame*. The semantic *interactions* between the focus and the frame are what allow or fail to generate the metaphor. The effort to recognise and interpret a metaphor is strongly dependent on the particular circumstances of its utterance. The efficacy of the metaphor is related to the desire of the sign producer to take the metaphor seriously, to entrust it to activate the analogies in the receivers' minds and to have the communication to depend upon and to be nourished by the analogy. This context-dependent interaction escapes simple rules of language.

Eco (1984, pp. 141–198) in his ample overview of the concept of metaphor over the centuries, provides his own interpretation of the foundational semiotic concepts behind metaphor. Whenever metaphors are not used to particularize or generalize through substitution of terms, similar to what synecdoche and metonymy do, metaphors put into relation two different collections (encyclopedias) of sememes (units of content) to which are

related confined sets of semantic properties. The sign producer chooses which sememes gain or lose semantic properties, guided by the universe of discourse or frame of reference and regardless of whether or not they are expressed in the linguistic manifestation (since they can be implied but still conceptually fundamental). However, the process is neither linear nor self-contained, rather the semantic properties “come and go” as the sign producer utters the metaphor or as the receiver acknowledges it. The available semantic properties define *similarities* and *oppositions*, which contribute to the meaningfulness and efficacy of the metaphor.

By naming something with another term, it denies this something of one or more of its qualities (Eco, 1984, pp. 157–198), even if the metaphor itself does not describe this phenomenon. However, this feature is what kickstarts the receiver to analyze the domains involved in the metaphor. The superposition (and the swap) of terms changes the meaning and the implication of the terms in their own network of semantic properties: the semantic properties that do not coincide perish while the common ones are reinforced (the concept of “condensation”, Eco quotes Freud). The metaphor (or the analogy included in the metaphor, as further described in Chapter 4.3.2) can be described in its semiotic mechanism in terms of the acquisition and loss of semantic properties.

When the metaphorical swap of terms happens, the receiver establishes connections between branches of the hierarchies of sememes in the domain (Eco, 1976, pp. 279–286). In this activity, the contextual and circumstantial selections of elements are frequently switched and overlapped, and imprecisions of many kinds happen so that the connections between concepts result to be unpredictable. Especially when the sign producer establishes connections rapidly and joins very distant sememes in the domain, the receiver perceives psychologically a “jump”. The receiver can confusedly fathom these connections to be legitimate, nevertheless the receiver fails to detect

with clarity the series of steps in the underlying semantic chain linking the apparently disconnected points together. At that point, the sign producer perhaps showcased quickly the possibilities of interacting with the semantic system, but for the receiver the process is still something vague and indistinct. On the other hand, if both the sign producer and the receiver become equally aware of the path taken, they will be able to interconnect the semantic units, and the rhetorical process becomes a new authorized form of knowledge, or at least a way to challenge the acquired knowledge.

On this line, Black (1962, pp. 38–47; 1982, pp. 55–66) provides a further focus in the discourse on the metaphors' working, introducing the concept of the *interaction view* of metaphor, which is of great interest for the design of artifacts and also for the relation between metaphors and scientific models. A metaphorical statement has a *primary* subject and a *secondary* one, which are systems of concepts. A metaphor applies to the primary subject the implications characteristic of the secondary subject. The relationships between the meanings of the corresponding keywords of the two implication systems can be classified as (Black, 1982, p. 117): identity, ad hoc extensions, similarity, analogy, or complex metaphors implying subordinate metaphors. In the simplest forms, a metaphor limits itself to substituting or comparing concepts of the two subjects. However, in the more complex metaphors, the non-trivial ones, the meaning of the concepts *interact*: the new context (the *frame*) imposes a change of the meaning of the focus words of the metaphor, in a way that the receiver remains aware of both the old and new meaning at the same time. Each expression evokes a certain set of implied semantic meanings (*system of commonplaces*), which is a system of ideas that is not sharply delineated but sufficiently definite. Through these implications, the naive or the expert receivers produce implications depending on their sensitivity (including also half-truths and mistakes). This system is somewhat shared inside a speech community or society.

Metaphors indeed hardly share meaning across different societies. Not paying attention to these commonplaces while elaborating a metaphor will provoke an effect of paradox and demand justification from the receivers. However, if the metaphor suits both the systems of ideas involved in the interaction, the implied assertions made on the focal element of the primary subject will not be related anymore to the primary system, but to the secondary one: the implications will be *talked about* in the language of the secondary system, which will be rendered prominent and they will not be pushed into the background anymore. This is the metaphorical transfer process. This interactive process suppresses some details and emphasizes others, resulting in the reorganization of the receivers' view of the focal element of the metaphor. The metaphor filters the network of semantic connections, the focal element from the primary subject is seen through the metaphorical expression, and it is projected on top of the new context from the secondary subject. Since this process is very context and culturally dependent, there is no simple rule for applying the shifts of meaning, and therefore no convenient reason for why some metaphors work and others fail.

We could say that the concept of *universes of contents* from Eco can be assimilated into the concept of the *system of commonplaces* from Black. Eco (1984, pp. 177–187) proposes a model for the description of universes of contents that are bound to the terms (sememes) involved in the metaphor. The author proposes to describe these universes in the format of encyclopedias, meaning a potentially infinite network of properties of which ones are interpretant of the others without any being metalinguistic construction or semantic universals. Assuming unlimited semiosis and unlimited interpretation, each sign (linguistic and otherwise) defines and it is defined by other signs (linguistic and otherwise). This kind of encyclopedic representation can describe the concept of similarity and differences between properties in semiotic terms. Similarity between two semantic properties is described as the fact that in a given content

system these properties are named through the same interpreter (verbal or non-verbal). The same is valid for the differences, but the implied relation is the opposite of the similarity. Similarity and difference can be named by taking into account for example the agent subject, the object on which the agent acts upon, the counter-agent, the instrument used by the agent, the purpose or aim of the action, etc. For example, in the Machine metabolites and gears are *similar* with respect to being *ordered* in chains, but they are *different* in the way they *transmit* quantity (of motion and molecules). Given the possibly infinite semantic properties that the encyclopedias can include, a subset of semantic properties appears to become more relevant depending on the identification of the topic of discussion and a potential path of interpretation. Moreover, reference frames or intertextual scripts could support finding what is being talked about, with which intention, direction and to what ends. Most likely, the encyclopedia will not be readily exhaustive for all the possible fruitful permutations of properties, but it will become exhaustive bit by bit through the exploration of metaphors which make use of those properties. The conception and development of the metaphor is dialogical, between the interlocutors and with the encyclopedias they come up with. Iteratively, taking various semantic properties as progenitors of new semantic representations leads progressively to broaden the scope of the encyclopedia. The better metaphors are the ones which do not allow the inspection to be stopped, and that support different, complementary and contradictory inspections.

The representation of the Machine de Lejeune goes in this direction: it provides a variety of visual inputs that are not quite fully described. It is a curious fictional contraption, with its own metaphorical rules of working, many of which are not explicit and that refer to a domain (biochemistry) which is fundamentally invisible. The visual analogy and its visual metaphor are rich but not exhaustive, it entices the reader to know more and to

speculate further on the Machine, while in fact the speculation still happens in parallel on the biochemistry units of contents.

A metaphor which is conceived *interactively* (in Black's terms) and not merely as a literal translation of terms, is a distinctive cognitive operation requiring the receiver to make use of a system of implications to select, emphasize and organize relations in different fields. The use of a secondary subject to foster insight into a primary subject demands the receivers to apply simultaneous awareness of both subjects. This is why metaphors are worth being inspected and used if the occasion arises, because they stimulate ways of reasoning and inferences that are fairly common in the experiences of learning anything new.

In the Machine the Lejeune, metabolites are rendered only for what concerns specific properties: their concentration, their belonging to a pathway or an enzymatic reaction, their main function in relation to the maintenance and development of the high functions of the mind. Every other property is suppressed by the Machine model: the structural composition of the molecules, the biology of their generation and transportation, etc. The metabolite concentrations (the focal point of the primary subject) are described as gears in the Machine. The biochemical interaction between metabolites then is talked about in the *mechanical* language (the secondary system), their imbalance is conceptually represented as a mechanical malfunction. At the same time, the representation of the pseudo-pascalian machine and the arrangements of its components, the "metabolite gears" (an actual metaphorical expression), is organized in function of micro and macro biochemical phenomena: on the micro-level, the gears are made contiguous or linked via pulleys basing on the known biochemical pathways; at the macro-level, the reference frame imposed to the representation system filters and organizes the clumps of gears into four main fundamental biological functions. This is the interaction view of metaphor in the context of the Machine the Lejeune, both the domains undergo a reorganization of their semantic structure

in force of the metaphorical interaction. In turn, the metaphor generates a novel meaning for the description of the problem at hand, proposing in this case also a heuristic view for his possible solution. Once properly understood the visual metaphor, it is difficult for the reader to go back to the abstract notion of molecule concentrations when looking for the root cause of where the “machine does not work as intended”. But metabolites have never been mechanical gears, and yet it is much harder to conceive the notion of “imbalance in a precise and deterministic organism” if we look away from the mechanical model of Lejeune. The visual representation is not a fully functional machine, it is the abstract model of one. And yet, it serves its communicative purpose as a (visual) language tool. It does not follow all the mechanical laws which make a mechanical device work in reality, but only a dedicated subset that is functional to illustrate the inferences on metabolite concentrations.

Summarizing from Black (1982, pp. 114–119), in the context of a particular metaphorical assertion the two subjects *interact* in the following way: (1) the presence of the primary subject entices the listener to select some of the qualities peculiar to the secondary subject; (2) at the same time the listener constructs a parallel “system of implications” that may fit the primary subject; (3) the implications reciprocally induce parallel changes in the secondary subject. There is similarity (analogy) or identity of structure between the set of secondary implications of a metaphor and the set of assertions (the primary set of implications) to which it is applied. It could be said then that each metaphor mediates an analogy or a structural correspondence, implying an assertion of similarity and an assertion of comparison, each of which is weaker than the original metaphorical proposition. Metaphor, however, as illustrated by Black, is not a mere comparison; it has a strength of its own, which is to impose the primary *subject's point of view* (its *implications*) on the secondary subject. The fact that a metaphor presumes some kind of analogy to manage the

relations between the sets of concepts between the primary and secondary system, leads us to the next section.

4.3.2. Analogy

In their treatise, Perelman & Olbrechts-Tyteca (1966, pp. 393–420) provide a comprehensive introduction to the rhetorical device of the analogy. Analogy is commonly associated with the proportional relationship between two domains ($A:B=C:D$), even though it is more in general a comparison between what is similar and what is different in the relationship between the two different domains. The authors define the domain of $A:B$ as the *theme*, whereas they define the related terms $C:D$ as the *phoros* of the analogy. Usually, the sign producer is more versed in the phoros, even if it is not a rule, showing an asymmetry of the space which is dedicated to one domain over the other in the argument. The choice of the terms to put into relation between theme and phoros can be performed by differentiating them by nature (horizontally) or by order (vertically), and the quality of the relation determines the readability of the structure of the two domains in parallel. An important notion is that the relationship of terms between theme and phoros does not imply that there was a previous relationship between those terms. Relations can be made up, explored and expanded at will, especially in those analogies that are rich. Moreover, the relations are not bound to be of mathematical proportion. The nature of the chosen terms is never neutral, they always influence each other reciprocally, to the point that the terms from the phoros can enlighten or tarnish the interpretation of those of the theme. Interestingly, often while thinking about an analogy, the reciprocal influence of the terms leads the sign producer to include in the structure of the phoros some concepts which would otherwise fail to find a semantic collocation in the phoros domain if not because they emerged while thinking on the theme

domain, in which they would have meaning. The authors remark how especially when the phoros domain pertains to the tangible reality, whereas the theme domain pertains to abstraction or spiritual matters (both by definition difficult to describe in terms of structure), the analogy serves to (re)build the theme domain with a plausible structure.

The authors illustrate the different purposes of the analogy as a way to debate: invention or proof. When the analogy is used for invention, there are no limits to its exploration: the analogy can be pushed to its limits and then collapse; whereas, if the analogy is used for proof, to convince someone of its validity, its exploration should end before it becomes untenable in debate, not least because it lends itself to counter-arguments. Interesting to notice how the authors describe the use of analogy in natural sciences: in natural sciences, the analogy is used mainly as support for creative thinking; at some point, the scientist attempts to overcome the analogy by reaching the conclusion of a similarity. This would grant the possibility of applying the same concepts and inferences to both theme and phoros. In doing so, theme and phoros collapse in on themselves, becoming a single field that can be investigated using the same methods. Analogy is a stage of inductive reasoning and by extension of scientific enquiry, where it serves as a means of invention rather than a means of proof. If an analogy is particularly fruitful, the theme and phoros are transformed into examples of a more general law, which unifies (but no longer looks directly at) the theme and the phoros. Any asymmetry between theme and phoros thus disappears. The success of the analogy in this field of application is to disappear.

The Machine is no exception to this customary use of analogy in natural sciences: Lejeune explicitly described it as a support to simplify the complexity of the problem and to direct sight towards the most promising investigations on metabolites. Still, the top achievement of such a model would be to favour the computation of the conversion formulas for every metabolite

on the map, and to transform such quantities into kinematic formulas for its fictional gears. At that point, if there would be a correspondence between biological and mechanical data, a theory could be posited, and the relevance of the analogy itself would fade, because it reached success.

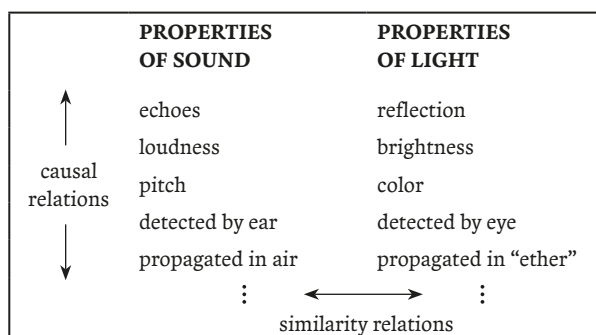
We can notice how many similar features are described by Perelman & Olbrechts-Tyteca (1966) for the analogy in comparison to what is reported in Chapter 4.3.1 for metaphors. Indeed, the two rhetorical devices tend to overlap and blur their boundaries noticeably. This impression is not trivial, metaphor and analogy serve similar purposes. The authors (Perelman & Olbrechts-Tyteca, 1966, pp. 421–432) describe the metaphor as a “condensed analogy”, resulting from the fusion of an element of the phoros with an element of the theme. Especially in the case of the fourth type of analogy of Aristotle ($A:B=C:D$) the metaphorical expression is indeed born out of an analogy. It is also quite infrequent that the two domains are talked about in a completely independent way, so analogy and metaphor can overlap frequently during a discussion. But there are several other kinds of metaphors, even if we do not focus on them in this dissertation. As mentioned in Chapter 4.3, it is functional to describe analogy as dealing more with the logical inferences (since it is more akin to the concept of mathematical relation) underlying the communicative layer of the metaphor. As the authors remark, an analogy is usually presented as a sort of fact, a datum, whereas the metaphor is used to provide credit to the analogy. Moreover, the frequent use of metaphors leads the properties of their theme and the phoros to assimilate each other into a new form of language (as Eco and Black remarked in the previous chapter), which makes the metaphor behave like a well-constructed analogy that gets assimilated into a more formal theory. However, the metaphor loses its spark of interest when it becomes customary, it becomes more and more overlooked.

A fundamental concept for the understanding of analogy is the concept of similarity, which acts as scaffolding for both metaphor and analogy. The previous chapter provides a theoretical and pragmatic definition of similarity. In brief, as Eco (1976, pp. 195–201) remarks, similitude can be defined not only as a shared set of properties between the object and its sign, but as a relation founded on some contextual rules which make pertinent some features and disregards others as irrelevant. If the posited rule is accepted, the motivation which puts into relation the two entities can be found since their similarity is not completely arbitrary anymore. This relationship of similarity though is not given, or even self-explanatory and it may require some training to be gleaned. A similitude is produced and must be learned, especially when putting into relation abstract visual contents of a model and representations, since the latter is the result of a cultural (design) decision and as such requires a trained eye to be detected as the representation of the object (content).

Mary B. Hesse studied in depth the logic and mechanisms of analogy, and she (Hesse, 1966, pp. 57–67; 1980, pp. 80–87) proposes ways to classify the analogies depending on the relation they describe. A common feature of the various types of analogies is the presence of horizontal and vertical relations between concepts. Horizontal relations concern *similarity* (i.e. identity and difference) while vertical ones concern in most cases *causal* relations (**Figure 25**). The type of analogy we observe more closely in the context of this dissertation is the *scientific analogy*, in which two lists of properties of concepts are put into relation by similarity. Sometimes terms do not even have correspondents in one list or another. In this type of analogy, it is not always obvious initially which property of the first list corresponds to some property in the second list, or if there is even no correlation whatsoever. In these cases, when some correspondence is lacking, the correlation can be invented, i.e. not observed, just postulated to fill the place (like the *ether* substance for Maxwell) and then investigated by observation later.

Figure 25

Reproduction of Hesse (1966, p. 60) diagram of causal and similarity relations between properties in two domains.



Given a way to model the sets of properties to put into an analogy, the author also provides a nomenclature to describe the correspondences between terms of two sets. Hesse (1966, pp. 8–9; 1980, p. 45) proposes a definition of the relational components of an analogy in the following way, taking as an example the analogy between the gas molecules (primary system) and billiard balls (secondary system):

- *negative analogy* of the model: the properties known to belong to the concept of the secondary system but not to the concepts of the primary one. The hardness, colour, and shininess of the balls are not to be ascribed to the gas molecules;
- *positive analogy* of the model: the properties known to belong to the concept of the secondary system which we *want to ascribe* to the concepts of the primary one. The motion and impact of the billiard balls are ascribed to the gas molecules;
- *neutral analogy* of the model: those properties in the model which we do not yet know whether they are positive or negative analogies. These properties raise the most interest because they are the object of new hypotheses and

predictions. In the example, if the billiard balls truly behave like the gas molecules, disregarding the properties in the negative analogy, by describing the behaviour of the billiard balls we might be able to hypothesize the behaviour of the gas molecules. If the hypotheses are wrong, the model is also wrong or there are some properties to be better described and classified.

The model founded on an analogy is an imperfect copy of the primary subject's phenomena, the result of the positive and neutral analogies without the negative analogy, which can be already discarded. The categorization of the elements of knowledge (*terms*) falling into these three categories is bound both to the scientist's knowledge of the domain, but also to the linguistic ability (and spoken language) of the scientist to notice the analogies and to be able to point them out. At that point, the description of the elements does not need further interpretation like mathematical terms require.

Another dimension of relation that characterizes analogy, which is closely connected with the type of relation, is the *mathematical proportion* (Hesse, 1966, pp. 64–67; 1980, pp. 85–87). Entities in the lists of terms sometimes can be put into a mathematical relation such as “*a* is to *b* as *c* is to *d*”.

$$\frac{a}{b} :: \frac{c}{d}$$

Describing the relation in these terms, binding them to a proportion with formal characteristics, allows the scientist to perform calculations, such as permutations and additions. This way, if some term is not yet clearly defined, the investigation proceeds as if the scientist is looking to find the fourth term of proportionality, given the other three terms. The possible results of this proportional relation depend on the vertical relation between terms. If the causal (vertical) relation between terms is

not yet known, the relation between terms has to be looked at by similarity (horizontally, across the two lists of properties).

Even if proportionality is the characteristic that commonly is used to describe analogy, proportion and analogy *are not* the same, they coincide only on some occasions. An analogy can yield multiple possible results for any given relation, with multiple terms corresponding to another one by similarity in different respects. Moreover, the vertical relation in analogy might not be proportional, therefore making it impossible to perform permutations without producing relations of different kinds. Moreover, lists of terms showing similarities between each other might not show the same similarity with a third list, in the same way and to the same degree.

For as fundamental as it is the relationships between terms to form an analogy, determining and defining causal (vertical) and similarity (horizontal) relations pose several issues (Hesse, 1966, pp. 67–87; 1980, pp. 87–100), since similarity relations are particularly problematic to define. When comparing two sets of terms by analogies (from two different domains), even though the sets might show some similar properties, those are never the same. Only some characteristics of a property might be shared, therefore to have a more precise description of the relation, each property groups its own set of characteristics (**Figure 26**).

Figure 26

Reproduction of Hesse (1966, p. 71) diagram showing relationship only of some characteristics of properties.

ANALOGUE x	ANALOGUE y
$A_1(x)B_1(x)$	$B_1(y)C_1(y)$
$A_2(x)B_2(x)$	$B_2(y)C_2(y)$
$\vdots \quad \vdots$	$\vdots \quad \vdots$

Note. A, B and C are characteristics of properties of both the domains involved in the analogy. The analogy in this case relates only to the B characteristics.

But even by modelling further the characteristics of the two sets of terms in an analogical relation, the process of description of the degree of similarity between terms is inaccurate, incomplete and inconclusive, since similarity can hardly become a discrete and differentiable construct. We can show some confidence in asserting the existence of a similarity between some things rather than others, but we cannot usually locate in an object some discrete characteristics which are surely and definitively identifiable with (or differentiable from) the ones of another object. In short, it is pointless trying to define degrees of similarity among the sets of terms. Though, this shortcoming does not make analogy useless, because it is not an incorrigible inductive method, but a method of selecting hypotheses. For the purpose of the analysis of models and their analogies, the horizontal dyadic relations between terms are relations of similarity where similarity can be reduced to identities and differences between sets of characteristics making up the terms.

Causal (vertical) relations are a bit easier to spot within the sets of terms. They can be of many kinds, for example whole-to-part, organism-to-organ, protector-of, obedient-to, etc. Usually, these relations are tied by co-occurrence, meaning that one term is a causal condition of the occurrence of the other, or that it promotes or inhibits the occurrence of the other. Through the reflection on the relevant causal relations in the analogy, the scientist tries to predict the occurrence of certain properties or events, or at least their tendency to co-occur. This is not guaranteed though. For as complex as it is to trace causality, for what concerns the nature and use of an analogical argument it is enough to express how if the analogical argument is valid, the same sense of causal relation should be carried over from the model to the *explicandum*—i.e. the description of the phenomenon to be explained, in extreme synthesis—in virtue of the relations between the characters which model and explicandum share. The vertical relations in the model are causal relations in some acceptable scientific sense, where there are no compelling

a priori reasons for denying that causal relations of the same kind may hold between terms of the explicandum.

The way Hesse describes the basic modelling for the characteristics of the two sets of terms put in analogical relation is close to what Eco describes for the organization of sememes in the encyclopedias involved in the metaphor (see Chapter 4.3.1). It is indeed tough to conceive an encyclopedia of semantic properties relevant to the metaphor topic and the desired context, and to define their internal relationships (vertical or horizontal) by means of some discerning criteria that are cohesive and not contradictory. To help in this process, Eco (1984, pp. 190–191) proposes a set of guidelines for the interpretation (and consequently the production) of metaphors, which covers also the choice of the semantic properties: (1) start by choosing a first version of the metaphor sememe of the first domain (partial, tentative), which supports the emergence of some semantic properties while suppresses others, to perform a first abduction; (2) Find out in the locally postulated encyclopedia another sememe from the second domain which shows similar semantic properties and also other seemingly interesting properties. If more sememes are good candidates, try out different variants by abduction using clues from the context; (3) select one or more of the properties which seem to belong to a common category that can be named appropriately; (4) the two sememes should be in an interesting relationship if the category which includes them is relatively at a conceptual high level. However, as also mentioned in the previous chapter, similarities and differences in semantic properties can be defined only by taking into consideration the context of the metaphor and its function, there is no formal criterion that establishes the correct degree of difference, and neither the correct conceptual level of the category which includes similar properties.

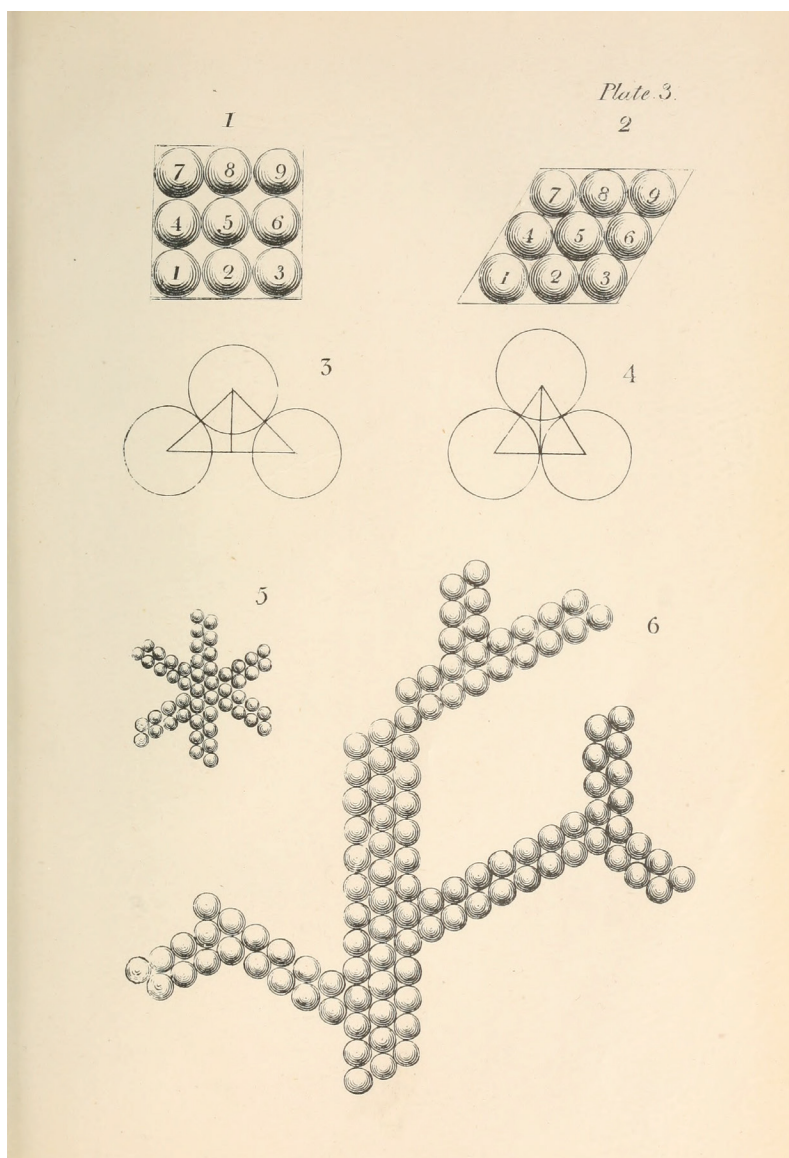
The difficulties described above by Hesse and Eco about modelling the characteristics of the two sets of terms in an analogical relation highlight the nature and limitations of a

visual representation as an analogical model in comparison to those scientific models which satisfy all the conditions for a predictive use to expand the theory itself. Hesse (1966, pp. 87–92; 1980, pp. 100–104) explains how a particular kind of model, the *conceptual models* (which significantly resonates with Johnson & Henderson, 2012) can identify relations of similarity (horizontal) and also can propose a neutral analogy which can be of use to postulate new predictions, but the model itself is completely *imaginary*, meaning that it is not realized in any existing or possible known physical system. The behaviour of the conceptual model can be a modification of an existing system or deduced from a causal theory. In this way, the model could also identify relations of causality (vertical). But if the model is not derived from any causal theory, and the hypothetical relations are completely imaginary, the model itself cannot produce reliable predictions in the domain of the explicandum and it cannot lead to the justifications required to state that the world (the phenomena) will behave like the model. Even though conceptual models cannot expand the theory themselves, they are imaginative devices to be modified and fitted to the data, serving the purpose of providing suggestions for the development of the theory. Hesse discusses how these tools played a key role in the history of science, and their use is a common mode of scientific reasoning, especially in the early stages of the development of a theory (like John Dalton's sketches of atomic combinations on paper, without knowing causal laws of the configuration of the atoms at the time. See **Figures 27–28**). Indeed, the conceptual models provide a means to give new interpretations to theoretical terms into observables that are not completely arbitrary, since they are bound to the language of the model itself. This makes them predictive in the view of the scientist.

More or less the same characteristics of the conceptual models apply to *analogue machines*, which are built to simulate the behaviour of the explicandum, even though they are not suitable to be a model for it.

Figure 27

Configuration of particles of water. Dalton (1808), Plate 3.

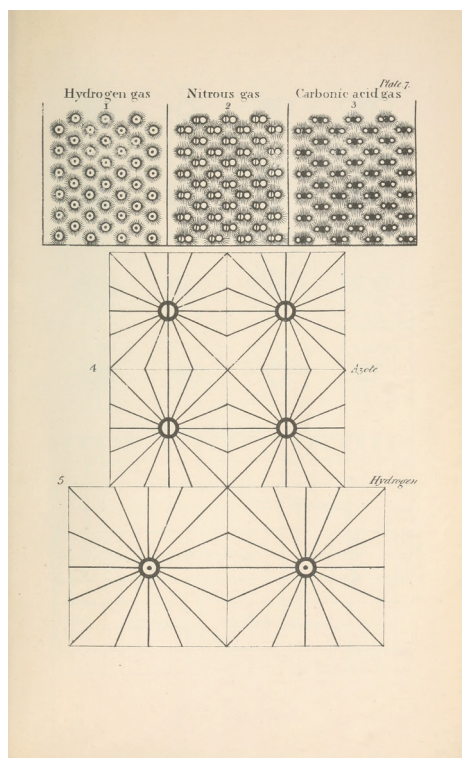
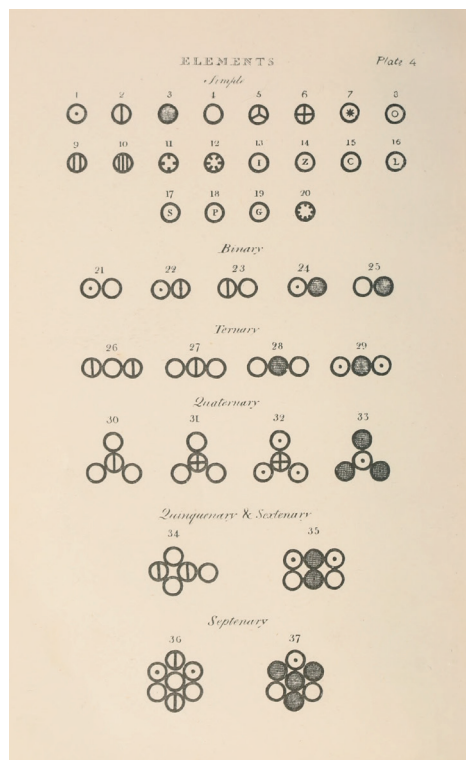


Note. (1) arrangement of particles of water, in a square shape, (2) arrangement of particles of ice, in a rhomboidal shape, (3, 4) different perpendicular sections of the arrangements, determining the volume of the strata of particles, (5) arrangement of particles in a small spiculæ of ice, (6) ramifications of ice at the beginning of congelation.

Figure 28

Notation for the representation of chemical elements, from Dalton (1808).

Plate 4 (left) and Plate 7 (right).



Note.

Plate 4: Dalton developed an arbitrary visual language to represent different atoms and their combinations in compounds. E.g. (1) Hydrogen, (2) Azote, (3) Carbone, (4) Oxygen, (30) Oxynitric acid: 1 azote + 3 oxygen, (35) acetous acid: 2 carbone + 2 water (1 oxygen + 1 hydrogen).

Plate 7: Dalton represents the arrangement of particles constituting elastic fluids. Profile views of (1) Hydrogen (2) Nitrous gas and (3) Carbonic acid gas. (4) Conceptual representation of particles of azote with their elastic atmospheres (rays emanating from the solid central atom). Since the rays are alike, they all meet to an equilibrium. (5) Representation of hydrogen atoms in proportion to the azote atoms in (4). Hydrogen atom's rays meet, whereas they do not meet with the rays of azote, causing the intestine motion of the mixture of these two elastic fluids until the mixture presses onto a solid surface.

Nineteenth-century mechanical ether models were not intended to reproduce the actual component structure of the ether, and electronic brain models were supposed to replicate the biochemical structure of the brain. However, they become useful predictive models when the material substance of their composition becomes the negative analogy, not essential to the model, whereas the behaviour of this substance becomes the positive or neutral analogy.

Looking at this framework, the Machine results being a very peculiar kind of model: it is a *conceptual model* since it is a visual representation of an abstract machine. It implies causal relations based only on some simple laws of mechanics and similarity relations with enzyme kinematics and other biochemical phenomena to determine the speed of the moving parts. However, the model refers to a *machine*, its conceptual behaviour is very much similar to the analogue machines from the XIX century, with the explicit intent to not reproduce the actual component structure of biochemistry but its quantitative interactions. As Hesse remarks (Hesse, 1966, p. 163; 1980, p. 151), in the mechanical philosophy conception, nature becomes similar to machine and concrete machines are seen as if they were stripped down to their essential qualities, i.e. mass in motion. The Machine is indeed an imaginative device meant to be fitted with data, to provide suggestions for a theory, but which cannot provide itself justifications for the phenomena.

This dissertation will not go further in the discussion of the logical problem of justification of analogical arguments since, as said earlier, the main interest of this dissertation is the communicative potential of analogies and metaphors, especially the visual ones, and the opportunities they provide to put into relation different domains of knowledge. Visual representations used as conceptual models can hardly provide the necessary complexity to encompass all the linguistic and formal terminology to compile a theory that can be also verified or falsified through logic. Visual instruments are indeed more of an

invaluable support in the process. More formal models, with known causal relations between the terms of the model, can withstand justification. Nevertheless, we can make practical use of these notions about the relationship between analogy, metaphor and models, to plan and shape the design of a visual artifact keeping in mind what are the elements of knowledge which are being represented, and to hypothesize their appropriateness for illustrating the original phenomenon. The next chapter will illustrate the core concepts of this complex relationship.

4.3.3. Models

As briefly mentioned in the previous section, the communicative intent of producing a visual analogy might not be to expand a scientific theory but to support the scientist in making inferences on the object of study. The inferences on the theory or the theoretical model might even escape the visual model while being still valid in the overall linguistic description of the metaphor and analogy embracing the model. Indeed both Black and Hesse express how pictures/representations might or might not fit the notion of model. A model can be buildable, picturable, imaginable, or nothing of such. Hesse (1966, p. 19; 1980, pp. 54–55) points out how some theories are surely not *picturable* (like the three-dimensional space curved in the fourth dimension for the theory of relativity). Black (1962, pp. 232–233; 1982, pp. 82–83) remarks that the power of a model does not lay in its capability to replace abstractions and mathematical formulas with forms of representation that can be readily visualized. Visualization can be a way to produce a model for those domains which are especially tied to abstractions, but visualizations alone do not warrant more fruitful inferences. Depending on the kind of phenomenon object of the model, sometimes attempting to visualize it is more counterintuitive than describing it through abstraction or calculus. Quoting the author: “To make good use

of a model, we usually need intuitive grasp ('Gestalt knowledge') of its capacities, but so long as we can freely draw inferences from the model, its picturability is of no importance". The main challenge while defining a model is therefore to not imagine (envision) the problem in an easier way, but to make the properties of the problem better known to the scientist in comparison to the ones directly related (or observable) to the original domain, to draw inferences from the description of the model, to control the implications of the model, to master the logical passages from one aspect of the model to another.

Even though visualization is not fundamental to models, the analysis of the concepts of metaphor, analogy and scientific models are of great use for the design of visual artifacts for science and biology. It is worth noting the importance of the analogical way of thinking in its various forms for scientific thinking, as they probably are the highest example of the meaningfulness and complexity of the thought that these rhetorical instruments can support. Not coincidentally, scientists often communicate and discuss in terms of models (Hesse, 1966, p. 55; 1980, p. 79), and even if this is just no more than uniformity in the scientific endeavour, it is surely worth investigating how to support this dialogue.

Metaphors are powerful communication tools with the capability to put into relation two fields of knowledge. This potential becomes a key thought instrument in science. Black (1962, pp. 219–243; 1982, pp. 67–95) extends his interpretation of metaphors to the concept of models, or rather "archetypes", and their use in science. These reflections are of great practical interest to understand the role the metaphors and analogies play in directing one's enquiries into not yet perfectly charted avenues of research, and also provide a glimpse into how design artifacts can support such process of discovery. As it becomes visible by the reflections hereafter, Lejeune as a scientist followed this process more or less explicitly.

Black then summarizes the key conditions for the use of a theoretical model: (1) there is a primary domain of investigation in which some facts and regularities have been established and articulated in some form so far, and (2) the scientist feels the need to master further this domain (to explain, understand better or expand further the regularities, patterns, corpus of knowledge and conjectures, or to connect the domain to other fields of knowledge); (3) the scientist then describes some entities (objects, systems, mechanisms, structures, etc) belonging to another more familiar or better organized secondary domain. This more familiar domain might indeed not be a realm of common experience, but a more thoroughly explored theory that the scientist knows how to use. The description of the properties of these objects is functional to whatever degree seems more useful; (4) the scientist posits explicit or implicit rules of correlation for translating statements about the secondary field into corresponding statements about the original field; (5) the scientist elaborates inferences from the secondary field which are then translated through rules of correlation in the primary domain. These correlations are then independently checked against known or predicted data belonging to the primary domain. This process of inferences connecting the described model and the original domain parallels the same process of inferences between an analogue model and its original.

The author keeps on describing that, of the various kinds of theoretical models in scientific research, the *analogue models* are artifacts involving a change of medium designed with the purpose of reproducing the *structure* of relationships of the original phenomenon as faithfully as possible in the new medium. Since the analogue model is a symbolic representation of the real phenomenon, the reader has to perform an interpretation of the relevant features of the phenomenon to make accurate inferences. These theoretical models differ from *mathematical* models in the way that they entice to find *causal* explanations, while mathematical models can provide a *form* of that explanation

or empirical assumptions by choosing the functions which can better approximate and fit the data. The pragmatic mindset of willfully not rushing towards premature theories and formalizing mathematical abstractions is at the core of the conception of the scientific use of theoretical models. The example of Clerk Maxwell's analogy between an electrical field in terms of the properties of an imaginary incompressible fluid is commented by the scientist as a way to simplify and reduce the results of studies *in a way that the mind can grasp them*. Relying solely on mathematical formulas can lead to defining laws but it makes the scientists lose sight of the physical phenomena, preventing them from extending their views of the connections in the subject. For the scientist, making a model is a way to achieve a physical conception of the phenomenon that is both intelligible and applicable to physical problems, while preventing him from formulating a premature theory. This leads Maxwell to conceive the electrical field *as if* it were filled with a material medium. This predisposition to conceive problems in physics through and by means of an underlying analogy is shared by other notable theorists (like Kelvin, Rutherford, Bohr, etc). At the core of this way of thinking there is the act of talking in a certain way: the use of theoretical models consists in developing a new language/dialect. The model does not need to be built, it is enough to describe it. This new language talks about a familiar theory extended to a new domain, while changing the representation of the new domain entices the further investigation of the original object of the inquiry.

The creative aspects of the metaphors (Black, 1982, pp. 133–135), for which they can act as cognitive instruments to reach new visions on a domain, are supported by the fact that “strong” metaphorical assertions (ones which are not ornamental or superfluous but founded on the interactive view and analogies) can be verified in the context of scientific research: since they express facts, it makes them susceptible to rejection and contradiction, as much as confirmation by supporting evidence.

This makes the representational aspect of the metaphor comparable to other acts of representation, like cartographies, maps, graphs, pictorial diagrams, photographs, “realistic” paintings and above all models, which are common cognitive tools to represent how something actually is, and not assertions on facts, and they can be evaluated for their correctness.

The set of features shared between the model and its original are not tied by an identical proportionality of magnitude, but the same structure of relationships, isomorphism. The nature of this relationship is what makes it possible to elaborate endless analogue models of a given set of contents (the phenomenon at hand). Isomorphism can be made explicit, and analogies can be evaluated for their appropriateness, faithfulness, partiality, superficiality, etc. The metaphors which survive such critical examination provide profound insights into the systems to which they refer. What makes this relation appropriate is to not open up to grave fallacious inferences, irrelevancies and distortions, and this should be independently confirmed by research of data in the original domain.

Correctness of the relations between analogous terms does not imply the possibility to provide proof for the theory. This analogical conception of the model has the drawback of the absence of explanatory power. This is what the physicist Pierre Duhem criticized the most (Hesse, 1980, pp. 44–46) addressing the use of models (mainly the mechanical ones) as an unnecessary distraction from a logical order, even if they can act as useful psychological aids to discovery. For him, the ideal theory is efficient and systematic, devoid of any analogy to more familiar (mechanical) models or imaginative representations. From the arguments of the authors Black and Hesse, it emerges that theoretical models are not a substitution for mathematical formulas (or more formal theories), they play a distinct role in scientific inquiry. Analogue models do not provide proof, the hypotheses suggested by the analogy must be verified through empirical investigation. But they provide plausible hypotheses,

that are indeed a key part of the scientific work to formulate theories. To be able to explain phenomena through a theory, the theory requires an intelligible interpretation in terms of a model, in addition to the formal and mathematical interpretation. Moreover, in the scientific context theories are dynamic, they are worked on and extended to embrace new phenomena. Without a model to make analogies with, extensions of the already posited theories become too arbitrary, as much as to make predictions in new domains of phenomena, which is one of the most important purposes of a theory.

5.

Implications for the design of visual artifacts for scientific explanation

In this chapter, inputs from the previous chapters are collected and synthesized, which can prove useful to the designers during the analysis and the design of conceptual and visual metaphors or analogies. The concepts are grouped depending on a common theme, developing a general *checklist* of implications to control when dealing with metaphors and analogies. All the topics are discussed fully and in-depth in the previous chapters.

A general concept that is applied throughout the guidelines is that it does not really matter if the designer is analyzing an artifact produced by other authors or if they are designing an artifact involving metaphor or analogy: the attention to pay to the various points is the same. Indeed, even by conceiving from scratch a design, the designer dialogues within him or herself and with the problem to represent. The designer must at all times be attuned to control the implication of the analogy he or she is adopting, to avoid misconceptions and to prevent the readers' misinterpretation. Checking our own metaphors or the ones proposed by other people is founded on the same critical endeavour. For this reason, analysis and design are not explicitly told apart in the guidelines, they are always assumed as part of the same intellectual effort. The difference lies in the output of

the work, which in the case of analysis is the debate, in the case of the design activity is a design product.

The guidelines are provided sequentially, but they are not to be conceived as consequential. A great part of the complexity of working with visual representations which include analogies is that all the facets of the design problem are always there, all concurrent at the same time, overlapping to the point of making any analogical representation a challenge. After all, as discussed in Chapter 4.3, analogy and analogical reasoning, the task of creating meaningful analogies and metaphors is complex even starting from a linguistic and semiotic point of view. The visual language does not solve in and of itself this intrinsic complexity, it replicates it as any other language would.

ORIGIN

Metaphors are pulled from the cultural memory of any of the interlocutors, and they are expressed through the languages that the interlocutors know. Metaphors must be part of the interlocutors' cultural context, prior knowledge, expert or naive that is.

The fundamental effort the designer can perform is to find and then explicitly describe the source of the visual or linguistic metaphor. In the case of metaphors for scientific explanation, this task might require a significant amount of effort to collect the required fundamental knowledge of the domain and to understand which is the relevant information. Most likely, this endeavour needs to be supported by specialists in the domains included in the metaphor, since the more detailed and complete the description of the elements of knowledge to be related, the more fruitful the metaphor is likely to be.

To which cultural environment does the metaphor seem to stem? Does it rely on common everyday knowledge, or does it sound like a part of a niche or a specific domain of study? Who uttered it? Was it proposed by an expert in the field or by somebody

who can be deemed as a novice? Did the subject who proposed it seem expert or knowledgeable only in one or both the domains put into relation by the metaphor?

In case no precise information is available, it is worth making a hypothesis on the origin of the metaphor. It is important though to expose this hypothesis towards the interlocutors and to elaborate on it. This allows the interlocutors to critically reflect and argue about the implications arising from known or unknown sources of the metaphorical message. This sets the basis for further speculation and analysis.

Focusing on the visual metaphors for scientific purposes, the search for the philosophical or scientific reasons for which an author came up with a visual metaphor or analogy might not be a process of granted outcome, or readily available as much. If the authors are still available, as designers we can issue a polite request towards them or their close collaborators for an interview on the artifact, which can lead to uncovering details and implied meanings of the artifact that were previously unknown to the public. Alternatively, or even better as a complementary research effort, an on-field enquiry at the laboratory premises in which the artifact is discussed, following a more sociological or ethnographical modality, can strengthen the understanding of the meaning that the artifact plays in its context of use. This meaning could also diverge from the original rationale developed by the researcher who first ideated the metaphor and its representation.

On the other hand, the authors might not be available anymore to answer the questions on the metaphorical or analogical representation. In addition, the documents in which the author describes the motivations and rationale behind the representation might not be even publicly available. In this case, the investigation of the artifact becomes nearer to a literature review or research through archives. The organized corpora of the attributed authors' works can sufficiently enlighten the

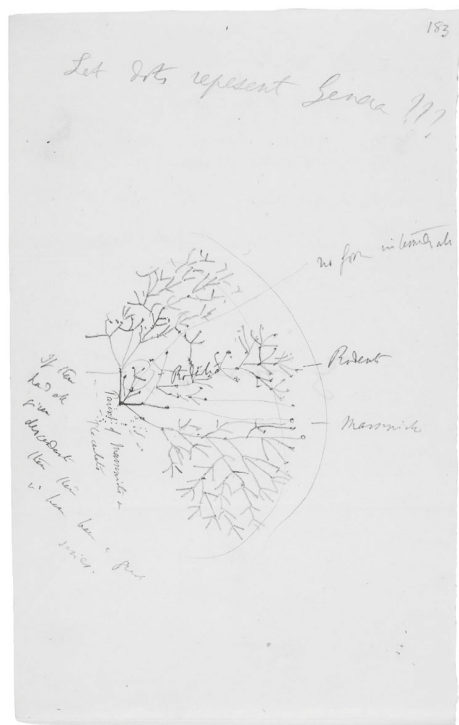
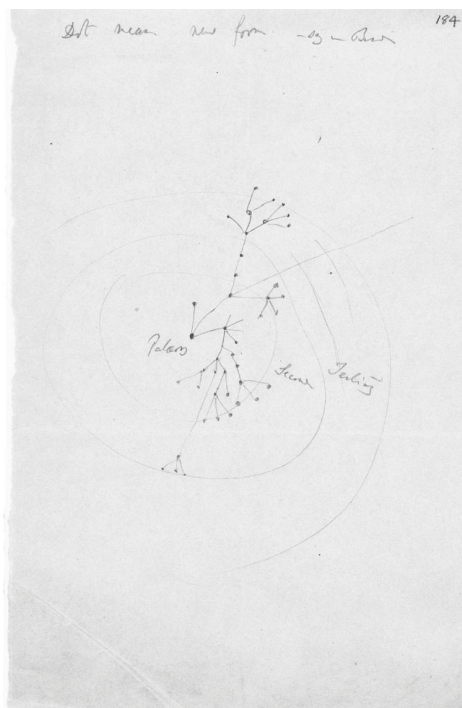
designers about the logic of the representation and guide them in the analysis. Most likely information gaps will emerge, parts of the representation which are not fully explained and become the subject of hypotheses and abductive logic. Fortunately, the metaphors are also meant to leave open spots for the reader to elaborate independently. The same goes for the representations since they impose a choice of visual language (which cannot be exhaustive by definition). In the luckiest cases, the authors provide ample notations around the representations, including also evolutionary drawings depicting the genesis of the hypothesis towards its more formal declaration as model. For example, Archibald (2014, pp. 80–112) (**Figure 29**) does splendid work collecting drawings from Darwin, in which emerges the iterative thought process of the scientist while still in the works of his model for organisms' evolution, and how he used his sketches as a support to envision the process, not the pattern, of how he perceived evolution to operate (Archibald, 2014, p. 112). In lucky cases, like for the *Machine de Lejeune*, the author issued publications discussing the representation and its implications, as much as infusing explicitly their view on the world in the explanations. These might be very unique cases, but the analysis of this documentation is fundamental to reaching a good understanding of the visual metaphor. This information, for as much as outdated or imbued with misconceptions belonging to the general culture of their times or their authors, is of the greatest importance. Beyond the basic explanation they provide to the designer, they make the metaphor (and the views driving it) verifiable to some extent, and therefore also falsifiable. By all means, the theories and hypotheses which moved the author could have been already disproven by the respective scientific community.

The traceability of the elements of knowledge and the falsifiability of their description and relationships create the basis for the instrumental use of the metaphor to explain or communicate effectively complex concepts while keeping a scientific profile to the discourse. As discussed before, a metaphor, an analogy,

Figure 29

Darwin's sketches of hypotheses on evolution.

Retrieved from Archibald (2014, pp. 88–90). A radiating tree (ca. 1857/1858) (left); a phylogenetic tree of mammals (ca. 1857/1858) (right).



Note. In the radiating three sketch (left), Darwin attempts to combine the visualization of evolutionary (ancestor–descendent) relationships with the notion of geologic eras (concentric areas from “Palaeoz”/Paleozoic, “Second”/Secondary, “Tertiary”); in the phylogenetic tree sketch (right), Darwin represents the mammalian evolution focusing on marsupials and placentals (rodents), hypothesizing “no form intermediate”, questioning previous theorizations.

and especially a visual representation including them, can evoke explicitly some concepts at high levels of abstraction or they can go down to more detail proposing analogies of proportion between phenomena in the two involved domains. Especially in cases in which the visual representation proposes analogical relations between quantities, not putting in relation qualities only, the representation implicitly suggests that there should be ways to verify said relations. The argument made by the author through the analogy results therefore strengthened, not only communicative but almost ontological.

FOCUS

The representation inevitably will not cover the full extent of the elements of knowledge and their complete relations within the domain. A selection has to be made, implicitly or explicitly. The criterion for which the selection is performed impacts the framing (as most likely this criterion is of a high level, imposing a reference frame or at least a high-level categorization). A simpler model is fine and perhaps even preferable as long as it matches the deep intent of the artifact's purpose. Expliciting the purpose of the model as best as possible, determines the appropriateness of the analogy, as much as contributing to the articulation of its traits.

In the Machine, Lejeune collects metabolites belonging to pathways more explicitly relatable to the nervous system and the functioning of a nervous cell. Many other pathways are left purposefully out, because they are not involved in the main hypothesis that an abnormality in the metabolism affecting the nervous cells is potentially the culprit for intelligence deficits.

Similarly, it is not fundamental that the universe embedded in the representation is coherent in all its supposed parts. What is not explicitly stated and left untold might not impact the perception of the model nor create misconceptions. The most important feature of the representation is its internal

consistency which must be supported by means of the analogy with the primary domain. The more the focus is made clear, the more the attention of the reader is directed towards the relevant features of the representation (positive or neutral analogy), the less the irrelevant features (negative analogy) should emerge. What the designer must remain aware of is to critically scrutinize each element of the representation that seemingly does not have an association with an element of knowledge of any of the two domains (especially the primary one). A graphic sign can be attributed with meaning by the reader in an uncontrolled way, so preemptive explanations on the usefulness or the irrelevance of that trait are the first failsafe against lingering misconceptions.

In the Machine, not all the mechanisms of the Pascalian calculator are represented. Quite the contrary, the representation is extremely simplified. Nevertheless, Lejeune clarifies in his publications the need for simplification and the information he provides is enough to focus on the heuristic value of the mechanical invariance of the geometry of gears, while suspending the elaboration on how those gears are put in motion.

COVERAGE OF THE ANALOGY

The act of developing meaningful analogies, metaphors and models is driven by the need to develop a shared language to describe a phenomenon that the interlocutors were not previously able to discuss. The model does not even need to be fully functional or complete, the important thing is to be able to talk about it. The new (visual) language contributes to extending the ability to enquire more about the domain or theory, to an extent that the richness of vocabulary the new shared language provides, and also to the extent the way metaphorical assertions can be verified in some way. Since the relation in metaphor and analogy is not meant to be identical in magnitude but to showcase the analogue structure of relationships, isomorphism can provide a measure to verify the analogy. Explicitly stating the

isomorphism criteria allows the interlocutors to critically examine the quality of the analogical relationships.

Did the author describe metaphor and analogy through sufficiently articulated language, such that one can test inferences on the basis of the shared language? Based on the descriptions and assumptions provided by the author, how can we set up a possible verification method for the metaphorical assertions?

It does not matter that the degree of similarity between the related elements is measurable by means of some mathematical proportion. What matters most is to assess how much dialogue the analogy elicits. Hypotheses may arise from the discussions of the interlocutors on the analogy, and these hypotheses will have to be evaluated in their own right, and not necessarily in light of the analogy that generated them.

DEPTH OF KNOWLEDGE OF THE INTERLOCUTOR IN THE SECONDARY DOMAIN

An appropriate understanding of the secondary domain is as important as the one of the primary domain. However, it is expected that the sign producer is more experienced with describing and dominating the implications of the primary domain, preceding the need for explaining and communicating elements of knowledge that he or she deems relevant. Nevertheless, interest in exploring the secondary domain is required to make a meaningful analogy between the two domains. An interest which should equal or even exceed the expected interest for the reader to acknowledge the analogy. The sign producer is in charge of putting extra effort into conceiving the analogy first, and then conveying it in a way that sparks curiosity into the reader. If the sign producer lacks curiosity in varied domains beforehand, not only fewer analogies can come

to light, but also the meaningfulness of the communication through the analogy surely will not be as effective as it could be.

The analogy does not have to go too in-depth, forcing relations between domains that are not logically sound and clear enough to the sign producer as a first. As we saw, on the contrary, the purposeful filtering of what gets in and what stays out of the visual analogy is the key to controlling the meaningfulness of the analogy as much as the lingering misconceptions that it can spark in the reader. The choice of what is meaningful and what “clicks” into the analogical relationship between the domains can only spark from genuine interest and curiosity in deepening one own's knowledge in different avenues of research and culture. This is probably the prerequisite for the whole process of analyzing or designing new metaphors and analogies (as much as their representation), which cannot be normed in a meaningful way by any supposed methodology. All in all, curiosity can be practised and perhaps also disciplined at the individual level, but not normed or prescribed in general terms. Thankfully, this is why the human mind provides endless possibilities to elaborate new and even unprecedented analogies. The best advice to designers in this sense is to be open and attuned to collect patterns and relations between information within interesting and stimulating domains, as distant as they might seem. Hard sciences, especially physics, show a long tradition of meaningful analogies leading to new theories, for example in the case of electromagnetism and fluid dynamics. Similarly, the habit of explaining problems in physics or chemistry in terms of mechanical machines was well established in the XIX century. Lejeune did not conceive his Machine out of thin air, the history of science provided him with an ample range of examples. The relation between the domain of mechanics and domains open to logical problems about unknown forces and quantities was not new. Those domains cannot be considered “distant” in light of what the history of science brings as an example. This is again to remark how in reality no domain should be considered by the

designer as totally unrelated a-priori, they are all open to the inspection of the designer and the scientist in search of converging patterns of knowledge. For as basic as this concept is, it is worth remembering it to counteract the ever-lingering separation of disciplines in confined epistemological and ontological distinctions. As we mentioned in Chapter 3.1, design makes its ability to act as a bridge between hard and soft sciences an identifying trait of its own discipline.

REIFICATION

The mode of representation of the metaphor or analogy can pose limitations or favour the elements chosen to be relevant in the analogical relation. For example, in the case of the GUI desktop metaphor, the digital representation allows for interactivity. However, this interactivity falls necessarily outside the scope of the functioning of the original analogue technologies used as metaphors. In the physical world, file cabinets, cardboard folders and windows do not behave like in a GUI. Conversely, a representation such as the Machine de Lejeune loses possibly the most important feature of the analogical relation, that is the dynamic motion of the gears, due to its static and analogue mode of representation. In both cases, the readers are challenged to infer some information that the representation does not provide itself due to its mode of representation. Imagining (and reimagining) the outputs of the design while being attuned and open to different modes of representation is useful to the designer to conceive metaphors that suit better their ultimate context of application.

What is the mode of representation? Analogue or digital? On which material? Does the representation focus on the interconnections between concepts, or is it more technically oriented due to the technological and market environment of its application?

REFERENCE FRAME

As anticipated in Chapter 2.4.1, in information design the concept of reference frame is strongly connected to the choice of using a visual analogy to expose and explain elements of knowledge of a given domain.

Summarizing from Bonora et al. (2020), the information design and analysis of a visual artifact can be informed through the four fundamental concepts of the synsemic writing (the *synsemic quatrefoil*): (1) visual variables, (2) dissociative variables, which define the visual hierarchy, (3) associative variables, which define the aggregates of graphic elements and (4) the reference frame. The reference frame is the conceptual and graphical device that is meant to activate in the reader's mind a context, and hopefully, the one which the author desires to evoke. In turn, this evoked context generates expectations in the reader on the functioning of the graphical artifact, and if said expectations are not met they can generate confusion or suspicion about the artifact.

The *context* emerges from the integration of the reader's perception, memories, actions which constitute a visual scene, a situation, a state of the memory. This integration affects the analysis of the artifact that the readers can perform, and the context activated in their minds supports or hinders their ability to assign meaning to the proposed visual materials. The reference frames act as “compressed contexts”: they are designed to degrade in a controlled way the “informational weight” of a complex context to make it “portable”, embedded in an artifact that can circulate on its own. This goal implies an operation of abstraction on the context: the designer reduces the number of explicit relations within the elements of the context, stripping the context of all the references that the designer hypothesizes to be accessory. The resulting scheme makes explicit those aspects that are considered more relevant by the author and the graphic compositor, while at the same time, the readers mentally

form their own reference frame, that is based on their expectations and previous experiences. Whenever the two visions coincide sufficiently, there is a good chance that the designed reference frame reaches the goal of enticing correct decompression of a relevant context that supports understanding.

In this dialogue between the mind of the author and the mind of the reader, as mediated by the visual artifact, there can be various degrees of compatibility (Figure 30): it depends on the combination of the number of relations made explicit within the reference frame and the degree of compatibility with the reader’s (conscious or unconscious) expectation of a graphical environment describing the context. When the reference frame is more “depictive”, since it explicitly proposes a high number of relations and finds high compatibility with the expectations of the reader, we can hypothesize that the process of reconstruction of the context performed by the reader is more regular and less resource demanding. Whereas, when the reference frame is more “abstract”, since it makes explicit only a small number of relations which though are highly compatible with the expectations of the reader, we can hypothesize that the process of reconstruction of the context performed by the

Figure 30

Description of reference frame types.

Reproduction of the diagram from Bonora et al. (2020), Table 1.

	High compatibility with the reader's “ideal-type”	Low compatibility with the reader's “ideal-type”
High number of explicit relations within the reference frame	Depictive	Impossible to disambiguate, inscrutable
Low number of explicit relations within the reference frame	Abstract	Hermetic

reader will be less regular and more resource demanding due to the more difficult interpretation. In cases in which the reference frame does not convey appropriate relations, and it results in low compatibility with the expectations of the reader, the process of reconstruction of the context fails leading most likely to incomprehension.

In light of this framework, we can state that an author who prepares a visual artifact including an analogy performs an attempt to enhance the chances to evoke a context that is more accessible to the reader. While moving a bit farther from abstraction towards a representation which can explicitly include more elements within its reference frame, the author seeks better adherence to the graphical and conceptual expectations of the reader. The effort which Lejeune puts into the Machine is to provide a scheme which the reader can use as scaffolding, through a visual language that provides visuo-spatial references to a phenomenon which is not otherwise easily representable if not through very synthetic and abstract notations (such as flow diagrams, or standard notation for the representation of molecules). The communicational gamble becomes then evident: either the reader attunes to the two contexts put into relation by the visual analogy (biochemistry and mechanics), or the alternative is to know abstract representations which impose the reader to rely on memory and procedural cues instead of providing a cohesive structure for the elements of knowledge that is more perceptible.

In addition to the issues in conceiving an appropriate reference frame, other problems might emerge in the way it imposes a layout to the representation, and how this impacts the reading of the contents.

Does the reference frame suggest particular ways to visually navigate the representation? Are these visual pathways the focal point of the discussion at hand? Should they be? Do they lead or mislead the reading of the user towards appropriate areas in the

representation? Should the relevant pathways be highlighted by the discussion on the artifact or with further visual notation?

POTENTIAL DEVELOPMENT AND EXPANSION OF THE ANALOGY

The concept of reference frame is strongly connected to the flexibility demanded by visual representations including analogies. Flexibility is also a proper feature of the analogy as a rhetorical device, which is its most powerful trait but that also creates expectations in the readers while they approach the visual information system.

Analogies are made to be explored, expanded, or discarded with ease depending on the communication goal of the interlocutors. Representations can do the same, but they can bear less “linguistic stress” since they require the development of a coherent graphical language to make any sense to begin with. An uncontrolled sequence of creation and dismantling of the structure of relations or the graphical choices for representing the elements of knowledge can seriously hamper the design effort to crystallize a shape for the artifact. As mentioned earlier, without a shape to converse on there can be no avenue for discussion. As designers it is worth looking a bit further while analyzing a given analogy: It could be beneficial to start planning out the layout of a simple case of visual analogy for explaining a confined problem. However, the effort in creating a cohesive reference frame and visual grammar can be scalable. It is worth speculating on how the analogical representation could be expanded by exploring the implication of the analogy at its basis. A significant benefit to the conceptual model comes when the model can be expanded and not rebuilt from scratch completely.

As shown in **Figure 9** and **Figure 10**, the layout Lejeune provided to the Machine is *expandable*. The more hypotheses are collected during the research work, and more areas of the Machine could be added. For example, adding further labels in

the reference frame would imply not only the rearrangement of the current gears but also new space for further metabolites to represent.

Does the visual organization of the analogy propose modular contents which depend on one or more fundamental concepts? Can the representation welcome additional elements in case the foundational analogy expands?

LANGUAGE PERMUTATIONS

Metaphors and analogies are basically logical mechanisms making use of language. The interlocutors' skills to make creative and meaningful permutations of terms in the language are tied to the ability to conceive metaphors and to perform analogical transfer of meaning.

Sharing between interlocutors explicitly the semantic path leading from one concept to another, and how the new meaning of the metaphorical terms in *focus* relates to the unchanged vocabulary of the *frame* should support minimizing misunderstandings, especially for the novice reader. At the same time, the interlocutors mutually should become able to uncover the system of implied semantic meanings (commonplaces) that they carry with them.

Amongst the vocabulary of terms collected from the two domains to be put into relation, which are the terms that are used metaphorically (the focus) and which are the ones that are used non-metaphorically (the frame)?

The ones used metaphorically need to be carefully checked by the sign producer and especially with the receiver, to acknowledge the shift of meaning that is most likely going to happen while using the metaphor. The reader remains aware of both

the original and the shifted meaning, and that is where confusion can arise. The sign producer should keep track of what is the metaphorical meaning of the terms (and visual representations) and their original meaning in the original domain, to not confuse the reader. As Hesse suggests, there are also ways to analyze the correspondences of properties of concepts, to control more finely the shifts of meaning between the two domains.

The *positive* analogy embraces all those properties of concepts of the secondary domain which the author wants to apply to the concept of the primary domain. The *negative* analogy embraces all those properties of the concepts of the secondary system but not to the concepts of the primary one, which ultimately are irrelevant to the analogy. The *neutral* analogy embraces all those concepts which the author does not know yet if they are positive or negative analogies. On the neutral analogy it is possible to make hypotheses.

Given the currently available information, is it possible to identify the positive, negative and neutral analogies in the correspondences between terms of two the two sets?

Salvi (2014, pp. 274–275) describes how emerging misconceptions can be of many sorts, but substantially they are all misinterpretations leading to incorrect inferences. It can also happen that correct inferences are made by unconsciously using a wrong model. In any case, it is important that the sign producer probes the receiver with questions (or even support materials, we can add) to let emerge misconceptions or the presence of a wrong model being used by the receiver. If the metaphor is of intuitive or incorporated type, it is harder for the receiver to explicitly state the elements of knowledge in use. In these cases, the effort of the sign producer should be greater in highlighting and explicating the analogies involved, to both enhance the potential of the metaphor and to prevent misconceptions.

On the other hand, if the metaphor is of formal/cultural type, the effort of the sign producer should be greater in verifying the prerequisite knowledge of the receiver in the source domain, to confidently produce analogies with the target domain.

Lejeune put noticeable effort in trying to prevent misconceptions in the readers of the Machine, explaining the “oversimplification” he embedded in the Machine, as a model to map the human metabolome and heuristically direct the sight of the researcher, without any claim to be exhaustive in the description of the complete working of a nervous cell. Lejeune established a dialogue on the artifact with his colleagues biochemists and less specialized audiences, both synchronously in conferences and asynchronously through publications. He produced versions of the Machine which superimpose information from other literature, which dialogue with other schemes from other authors and himself, he clarified the premises of the model and its potential implications, and he suggested perspectives on how to use the model that are still explored four decades later. These reasons suggest that Lejeune evidently conceived the artifact and the visual analogy to make use of it as a dialogical tool, less as an isolated act of reification of a thought process.

PERSUASIVE INTENT

Especially in the design of artifacts for scientific purposes, the ethical position and/or future vision of the author is embedded inevitably in the representation, making it become an instrument to persuade the interlocutor. Metaphors and analogies are particularly apt rhetorical devices in supporting this, since they are meant to close the gap between the message and the receiver. The people involved in the design take part in the vision embedded in the artifact, it is inevitable. The author and the designers should be aware of this, even explicitly stating these visions to provide the reader with the necessary mindset and critical tools while interacting with the visual metaphor or

analogy. This transparency supports the interlocutors in benefiting from the analysis of the artifact, mitigating the risk of a priori political or emotional rejection of the arguments. While narrating the Machine across publications and conferences, Lejeune often took occasion to remark on his motivations in pursuing his visions on healthcare and society. Even though he knew his opinions were controversial at the time, he was transparent about them. This enriched the debate at his time (beyond the scope of the Machine), but also he left us with reflections which are useful to better understand the visual artifact he designed. Years after the conception of the visual analogy, we can trace back the fundamental concepts to read it.

Is it possible to know or retrieve from literature the ethical views of the author? How do those views impact the choice of the elements of knowledge to visualize through analogy? Are these views too prominent and obscure the actual content of interest in the analogy? What was the historical context around the development of the artifact? How was it received by the critique of the author's peers? How was the author welcomed or opposed by the research community for the ideas expressed in his view?

If the representation involves a heuristic intent, it presupposes a method of measurement and validation, which in turn presupposes procedures that may already be standard or yet to be formalized. This can imply that the information structure of the visual analogy probably proceeds backwards from the measurement procedure, it does not impose the measurement. The data expressed by the visualization should be linked to a procedure that determines a verifiable quantity or quality. To get an understanding of this, the designer is required to understand the datum, its measurement, and the laboratory procedure that guides researchers to the retrieval of that datum. Without this effort, the resulting representation can hardly serve as a map for investigation, i.e. as a heuristic tool. Once again, the support

of the specialized personnel in the domains involved is fundamental to achieving such awareness. The procedure outlined in Chapter 6.1 is an initial tentative to work out the way to measure the quantities of metabolites of interest.

6.

Suggestions for further research

One of the objectives of this PhD project is to propose the basis for the future development of a computer model of the Machine, which could serve the biochemistry research community as a distributed and interactive access instrument to metabolism data. However, to do so, first the data must be collected and a plan should be conceived for the progressive prototyping of the computerized tool. In order to structure the collaboration between designers and specialists in genomics and biochemistry for the development of the digital model of the Machine, the me and the workgroup at the laboratory of genomics outlined the work plan as proposed in the following sections.

6.1.

Shared laboratory investigation procedure on metabolomics

DATA COLLECTION FOR THE DEFINITION OF THE METABOLOMIC MODEL

As a first step to creating a visual model that can work by means of mathematical computation, the workgroup must be

able to hypothesize (or even postulate) entities and relationships between data in a specified dataset. Therefore, the group decided to structure a systematic data collection process, which is aimed to catalogue in a database the concentrations of:

1. *Substrates* (i.e. chemical compounds) - the “gears” of the Machine
2. *Enzymes* - the “pulleys” and the “driving force/engine” of the Machine
 - a. Concentration data for each protein
or
 - b. Concentration data for RNA (it is perhaps a simpler procedure)

The problem with calculating concentrations is that by definition they are expressed as proportions. However, there are multiple ways to define the numerator and the denominator of said proportion. In this case, the group proposed to calculate concentrations based on the estimated number of cells in each tissue. The best outcome and product of this sort of investigation would be to obtain a table with the concentrations of all known substrates and enzymes in all tissues. On the other hand, this sort of data collection is time and resource-intensive. Even though it will be distributed over multiple researchers at the laboratory, as a starting point and to keep the effort realistic, the group decided to calculate concentrations:

- in just *two types of tissues*:
 - *Neurons*, a tissue which Lejeune himself focused on during his studies and a tissue particularly involved in the cognitive condition of people with trisomy 21
 - *Plasma*, as a means of transport for the metabolites
- in a specific *part of the metabolome*:
 - around the *one-carbon cycle*: e.g. TFH (tetrahydrofolic acid), homocysteine, methionine, transsulfuration pathway.

The basic structure for the data tables could therefore be as simplified in **Table 4**.

Table 4.
Hypothesis for data structure for the collection of metabolite concentrations.

Substrate data	Enzymes data	Conversion formulas
Concentration value	Concentration value	Formulas for the conversion of values from substrate to another substrate, based on the chemical reaction kinematics

In summary, the work includes a literature review for available data on each reaction (substrates and products, and transformation kinematics to estimate how much product is formed), and then the definition of an overall mathematical model of the cycle studied. Fortunately, there are already examples in literature of works covering partially this process for the one-carbon cycle (see for example Gnimpieba et al., 2011; Nijhout et al., 2004; Reed et al., 2004). The practice of collecting laboratory data and producing mathematical models for computer simulations is well-established in the field of biochemistry. Synthetizing from Duncan et al. (2013), the definition of mathematical models allows scientists to study *in silico* (i.e. reproduced in a computer simulation, as opposed to *in vitro* or *in vivo*) the relationships between metabolite values in tissues. This practice is particularly important to investigate metabolic conditions that are difficult to reproduce *in vitro* or *in vivo*. Through the model, the scientists can study the effects of variation in metabolites input, activities of enzymes in specific cycles (whether due to mutation, expression level, availability of vitamin co-factors, etc). The outputs of the models are then usually compared with known empirical findings from literature (e.g. concentration of metabolites in specific tissues of humans or compatible animals) to verify whether the model approximates the behaviour of living organisms. Indeed, currently the laboratory group is following up on the works of Misselbeck et al. (2019, 2017) on modelling

the folate-mediated one-carbon metabolism. As the authors show, quite sophisticated mathematical description is required to model even one pathway. The road to get a comprehensive of extended parts of the metabolism is still very open.

The laboratory group work plan for this phase unfolds as follows:

1. Write and share a protocol for collecting data from literature and previous experiments;
2. Structure the database, and carry out a pilot of data collection and storage;
3. Proceed with a shared, systematic data collection to distribute the workload.

DEFINITION OF AN UPGRADEABLE DIGITAL MODEL

The work on the mathematical model is currently proceeding at the Laboratory of Genomics. Once this mathematical basis is fine-tuned, the digital model of the Machine the Lejeune can serve as its graphical interface.

The digital version of the Machine de Lejeune should draw data from the database of concentration values and conversion functions. The database should be structured in a way that is intelligible to the research community in genetics and biochemistry. It will first be updated by the laboratory research group and then shared with the rest of the community.

The database itself, with its structure and values, dictates the form and functionality of the digital Machine. The group foresees that the digital model will most likely remain substantially faithful to the first paper version by Lejeune, but it may change in some parts given the scientific progress that occurred in the past forty years. The shared study of the Machine therefore embraces all its features, from basic data structuring to the subsequent definition of visual and formal aspects.

FOCUS ON THE ONE-CARBON CYCLE

As it happens for the data collection process on the metabolites database, also the design and technical creation of the digital version of the Machine will feature a defined and narrow scope: the first prototype will focus primarily on the one-carbon cycle, given the premises described above for building the first core of the database.

METABOLIC NETWORK SIMULATOR, PROOF OF CONCEPT

By structuring a database in the likes of what was described above, researchers could prospectively think about how to make use of these data to do simulations. By activating/deactivating/altering the values of specific metabolites or enzymes, the dataset and the interface could provide feedback on how the rest of the metabolism reacts: the digital Machine can showcase mechanical-kinematic variables (such as gear rotation speed) or visual variables (such as colour), while also the database itself can showcase variations in functions and variables.

While the laboratory group tries to understand how the metabolome data can be handled through numbers and formulas, from the design standpoint it is possible to try to build a very simple graphical model as a proof of concept. It might even be as simple as the animated rendition of two separate gears of the digital Machine, connected by a belt. The challenge is to understand if there is a computational way to associate the motion of these elements with numbers that determine their speed of rotation (as kinematic-mechanic variables) and/or their colour (as visual variables, mapping the concentration data with a palette that ranges from warm to cold colours perhaps). The chain of elements which is interested in a reaction is the substrate (the metabolite acting as “input”), the enzyme (the protein acting as “pulley”) and the product (the metabolite acting as “output”). All these components should work together perfectly if their

concentration is in balance. Abnormal concentrations of these elements should be associated with variations of kinematic variables or visual variables.

6.2.

A possible digital prototype of the Machine de Lejeune

The present PhD Project did not reach the point of making a new digital version of the Machine de Lejeune available for public use. However, during the PhD work, the workgroup jointly investigated motivations, possible technological solutions and overall development framework for subsequent developments of the research project. This chapter aims to expose these considerations, to make them available for a future community of researchers, designers and developers converging towards the creation of a functioning software system for the Machine.

MOTIVATIONS AND IMPLICATIONS FOR A DIGITAL MODEL

The object of interest of this research, the original Machine de Lejeune, is a communication artifact which was drawn by the author on an analogue media, a poster. However, the concept that Lejeune embodies in his representation is inherently near to what we could define as a “database”. Even if only at a conceptual level, the representation is *generated* by a set of values that are collected and retrieved to design a visual representation that users can operate to some degree. In the original artifact, the “database” of values is scattered in the scientific literature on the human metabolome and in the research notes of Lejeune’s workgroup. The prospective aim would then be to make the database interoperable using up-to-date technologies, and operable by specialized users through a custom Graphical

User Interface (GUI). In other words, there is a need to produce the computer model of the Machine that serves as a visual access instrument to metabolome data. The choice to develop a digital prototype of the Machine is a logical consequence of what I discussed in Chapter 4.2: the need to popularize and spread the subject matter within and even outside the biochemistry research community.

There are other motivations to develop a digital prototype which are functional to the research in the long run:

1. The need to test the functionality of the prototype with target users, which implies cycles of re-design. Even if it would be technically possible to produce numerous static and two-dimensional versions of the prototype, a more sustainable approach is to develop a mathematical and computerized model that is parametric, modifiable and at least dynamic, if not fully interactive;
2. The need to be open to adding new data coming from biochemistry investigations. Not all the data on metabolomics are already available. Without a mathematical model based on a database, it becomes inefficient to update the representation.
3. The need to have a digital model to manipulate its representation. The current way the Machine de Lejeune displays data might not be the optimal one when the representation is transferred in a digital environment. As long as data on metabolite concentrations are available, the digital model would provide the possibility to change the representation of the connected digital objects.

CORE VALUES FOR SOFTWARE DEVELOPMENT

Regardless of the technical choices of the programming language and platform through which to develop the digital prototype (for a preliminary proposal, see Appendix A), some core values determine the technologies involved. The

reflections proposed hereafter are both intertwined and independent from the actual technical solutions, because the reflections are grounded in an overall vision for a project on the Machine de Lejeune.

This dissertation and the Machine deal mainly with the dissemination of knowledge within the scientific community and the popularization of a research subject even outside its specific scientific community. The effort is to hopefully reach a broader and non-specialized audience with visual communication artifacts that compel action and research. The pulsing heart of this effort is to benefit society as a whole by providing contemporary tools in support of science and invoking discussion over socially and ethically important issues in healthcare and social inclusion. For these reasons, the languages used to produce the tangible (programmed) prototype artifact that incorporates this vision ought to be appropriate.

The development and the release of the prototype of the Machine de Lejeune should follow the ethical views of the free software movement (Free Software Foundation, 2021): to grant the users the freedom to run the code as preferred, to study the source code and to change it, and to redistribute copies of the code with or without changes. Developers take on this effort not just for the benefit of the individuals who will use the code, but for the benefit of society as a whole, promoting social solidarity in the forms of sharing and cooperation (Stallman, 2021). Sharing and improving codes as a community, and giving the community a chance to benefit from code changes is the preferred (if not only, in practice) way to ensure this research work will outlast any of the careers of the people initially involved in its development. Therefore, access to the source code can not just be seen as an ethical precondition for free software, but also as a precondition to the research. The source code is a research tool in and of itself.

This allows me to briefly disambiguate the concepts of “free software” and “open source”. These two concepts differ mainly

in the values that they incorporate respectively: free software is an ethical imperative to safeguard the users' freedom to collect, study, modify and redistribute the codes. On the other hand, open-source addresses more the practical side of how to make software “better” (through open sharing), but it does not take a precise ethical stance. In the words of one of the greatest exponents of the free software movement, Richard Stallman (2021), what the free software philosophy asks developers to do is “raising ethical issues such as freedom, talking about responsibilities as well as convenience, is asking people to think about things they might prefer to ignore, such as whether their conduct is ethical. This can trigger discomfort, and some people may simply close their minds to it”. This is what differentiates free software from open source. I do believe that this vision is very close to the function that a conceptual device such as the Machine de Lejeune operates within the scientific community. This vision transcends software development, it is a precise choice towards giving shape to contemporary and future society. I will not say that Lejeune's research adhered to such a vision, nonetheless he conducted his work on biochemistry to raise scientific questions, and to propose ethical stances even. Following the free software ethical guidelines to me seems just fitting to the ambitious task that first led this research to begin, about fifty years ago.

Indeed, the efforts in shaping the future of common well-being ought to be taken by a community of people working in the service of public benefit. Lakhani & Wolf (2005) surveyed a community of developers involved in free/open-source projects, represented in the sample for the majority by skilled and experienced professionals working in IT-related jobs, but including also students and academic researchers, with a whole group mean of about 12 years of programming experience. The authors inquire their respondents about what motivates them to participate in such kind of programming activities. Even though the developers were motivated by a combination of intrinsic and extrinsic factors, the strongest and most pervasive drivers of

their substantial efforts were enjoyment-based intrinsic motivation (personal sense of creativity), intellectual stimulation derived from writing code and improving programming skills, and the motivation to participate and contribute to the creation of a public good. I argue that the future of a project such as the digital prototype of the Machine de Lejeune will be carried on by a community driven primarily by those intrinsic motivators. The community will be put in the position to update and enrich the model with recent measurement data on metabolites, making the Machine an actual instrument for studies on Trisomy 21 and for all other genetic conditions which impact cellular metabolism. The software project should be released open source with a GNU free-software compliant license. Also because most likely good parts of the software components will be taken from the development community who released codes open source.

Following the principles for a free software ethic, a software development methodology which seems compatible with the above principles and that could become suitable to form the backbone of the community of development for the Machine could be inspired by the framework for hybrid-open source software communities by Sharma et al. (2002). Here it follows a summary of the relevant features of the framework:

- The division of labour is flexible and opportunistic: tasks within the project are not assigned to developers by formal plans, schedules or deliverables. Each developer chooses what to work on.
- The coordination mechanisms rely on decentralized work and asynchronous communication, given the online distributed nature of the collaboration between the developers, and the limited time availability of them. Teams are formed around problems and disbanded when the problem is solved. The supervision is provided by peers, and usually a core group of developers provide general strategic directions.

- The distribution of decision-making happens through asynchronous communication and voting within the team. Possibly the core group of developers could express binding decisions.
- There are no defined organizational boundaries and the structure is informal. Membership in the community is fluid, developers are free to join and leave as needed. By being open, the community exposes itself to a supply of constant new ideas and solutions. There is no formal organization structure, which changes depending on need. The actions of the volunteers shape the community and they carry out tasks informally under a general direction from the core group.

PROTOTYPE SCOPE AND LIMITATIONS

As already discussed in Chapter 6.1, the design and software development of the digital version of the Machine will include only a subset of metabolites and their chemical relations: primarily the one-carbon cycle. This choice is not related just to the constraints of the resources available, but it is a rational approach that also Lejeune himself followed before drawing the whole Machine. As already visualized in Chapter 2.4.2, **Figure 9**, in a publication (Lejeune, 1977) prior to the Moscow conference of 1978, Lejeune had shown a particular section of the Machine which focuses mainly on the metabolism part that deals with the production of energy. The first version of a potential prototype could look similar to that representation, but it could be focused more strictly on the one-carbon cycle. All in all, this approach intends to start small, make a proof of concept model, verify the assumptions, and then expand the model to other areas of the metabolome.

Appendix A.

Potential technologies for the digital prototype

In this appendix are collected those technical solutions I deem more promising for starting the creation of a prototype for the digital Machine, at the time of publication of the present dissertation. During the PhD work, I analyzed and tried different technological solutions, different development platforms, different programming languages and different libraries. I support the adoption of the technologies mentioned hereafter, because I am convinced that there are already communities of strongly competent developers who can contribute significantly to the project, with the right type of motivation (see Chapter 6.2). The technology proposed should also reduce at minimum the adoption cost from the biochemistry end user. However, I am well aware that the speed of change in development technologies, the turnover of adoption and abandonment of various frameworks by development communities, and especially the emergence of AI technologies could make this proposal obsolete in a short time. Nevertheless, the hope is that these insights will ease the start of the development process and, why not, they will ignite the curiosity of designers and developers not only on the Machine but also on other projects with the same free and open philosophy.

PROGRAMMING LANGUAGE

From a preliminary analysis of possible suitable technologies for the development of a digital prototype of the Machine the Lejeune, the JavaScript (JS) programming language (Mozilla Foundation, 2021b) seems the best candidate. JS is an interpreted, or just-in-time compiled, programming language which is mostly known as the scripting language for Web pages, even though it has pervaded many other environments including 2D and 3D graphic design software suites as a scripting language. JS is a prototype-based, dynamic and object-oriented language. It is based on ECMAScript standards specifications.

What is crucial about JS is that it can function as both a procedural and an object-oriented language (Mozilla Foundation, 2021a): objects are created programmatically by attaching methods and properties to empty objects at run time. Therefore, once an object has been constructed it can be used as a prototype for creating similar objects with equal or different properties and methods. JS does not need to be compiled beforehand to run in a browser: the JavaScript engines built in the browsers take care of reflecting the DOM (Document Object Model) into JS.

In the context of this project and its future derivations, these features make it possible to conceive how the digital prototype of the Machine could work: each part of the Machine is described by a blueprint, which defines the general aspects of the components and their basic interaction (rotations, hinges, and so on). In addition to that, each part can be programmatically (and automatically) customized in its simulated features and movements by data stored in a database via functions and methods that inject and convert data about metabolite concentrations into variables for the animated 3D simulation of the Machine. The web-based environment in which the simulation will reside is accessible frontend by just opening a webpage in a browser, while the backend is accessible by downloading the application

files and opening them with an IDE of any sort. For these reasons, the only requirement for frontend usage (by biochemistry specialists) is to install a web browser on their computer. For backend development, the initial setup of the workspace would be a bit more complex, but something that anybody with some experience with frontend JS web development and repository management/version control systems can engage with minimal effort. Even though different browsers include different versions of JavaScript engines (Mozilla Foundation, 2021a), those different engines refer to public JavaScript APIs, which contribute to keeping the results of the browser computations on JS codes aligned. For this reason, at this point in time there should not be any difference even about which browser the frontend users employ.

These features of the programming language, alongside its functionalities conveniently packed by the libraries I will illustrate right afterwards, contribute to the choice to use Javascript as the programming language for the development of the future prototype.

LIBRARIES

Two JS libraries are the main candidate to be used in combination with each other:

- **three.js** - JavaScript 3D library
- **cannon.js** - Lightweight 3D physics for the web

Both these libraries are released under MIT license, which is free-software compliant. This combination of libraries is needed to provide a simulation of a mechanical machine that can either run smoothly or jam. This feature of the representation is the basis of the analogy between biochemistry and mechanics.

Indeed, *three.js* allows the developers to use 3D graphics in a web environment (which usually is mainly 2D). It also allows the developers to script the movement of these objects in the 3D space. However, it does not provide a physics engine to the

scene. Every movement, animation and interaction between 3D objects has to be scripted by the developers and it will be executed by JS exactly as described. This is why the second library *cannon.js* should be added to the project. Cannon.js is a physics engine packed into a JS library, so that it can be used to make 3D objects interact as if they were in a specific kind of world with ordinary or custom physics.

three.js

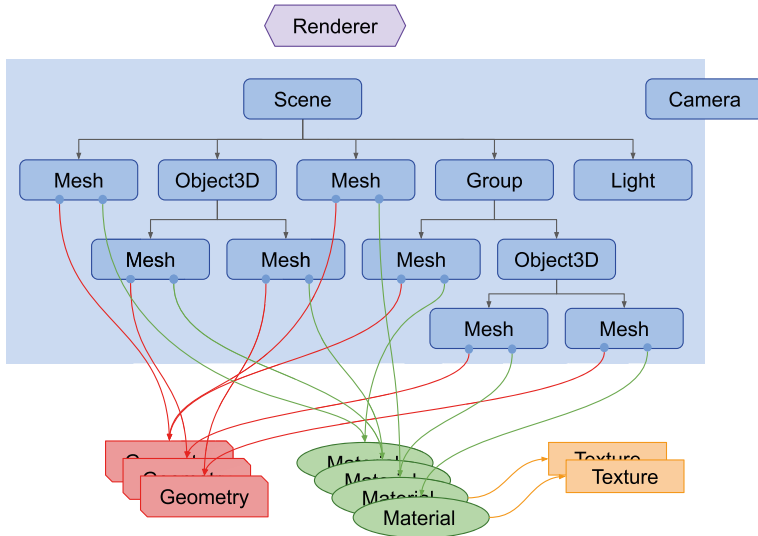
Three.js (<https://threejs.org>) is a JS library that makes use of WebGL technology to draw 3D shapes (mesh objects) and render them into an HTML canvas element in a webpage. In short, the library makes available a series of JS objects to setup of a three-dimensional scene and to manipulate objects within it. I will briefly introduce how it operates ([threejsfundamentals.org](https://threejs.org/docs/), n.d.):

- The *Renderer* object collects all the information from the objects *Scene* and *Camera* and it renders the 3D scene into the HTML canvas.
- The *Scene* object acts as a container for all the other objects to render, which can be:
 - *Mesh* objects, which are 3D drawings described mathematically by a *Geometry* object and which get their appearance from a *Material* object.
 - *Texture* objects allow for the loading of various types of images that can be applied to *Material* objects.
 - *Light* objects allow for the scripting of various kinds and sources of light in the scene.
- The *Camera* object dictates what the user can see on the Scene at any given moment. A *Camera* can also be scripted to be grouped with other objects, and therefore it will move with them. **Figure 31** visualizes the general scenegraph of Three.js.

Figure 31

Summary of the objects of Three.js and their relations.

Retrieved October 20, 2021, from threejsfundamentals.org (n.d.)



cannon.js

Cannon.js (<https://schteppe.github.io/cannon.js/>) is a JS library that allows developers to make use of a simple 3D physics engine. The library (Hedman, n.d.) was developed by Stefan Hedman in 2012 (based on the repository's history) as a response to the fact that the web lacked a physics engine. Indeed Hedman wrote cannon.js in pure JavaScript, inspired by other two libraries, *three.js* and *ammo.js*.

What cannon.js adds to a 3D library like three.js is the capability to compute the physics of the mesh objects in the 3D world (Hedman, n.d.), for example:

- Rigid body dynamics
- Discrete collision detection
- Contacts, friction and restitution

- Constraints, joints, locks
- Hinges (with optional motor)
- Collision algorithms for shapes like spheres, planes, boxes, cylinders and convex mesh objects
- Several other physics-related features

What is of utmost importance for the development of a simulation of a mechanical machine are indeed the colliders (or collision algorithms) and the hinges/motors functions. These mathematical functions allow the 3D shapes/objects (even compound ones such as gears, pulleys etc.) to act as if they were made of solid materials. In the prototype of the Machine, the movement of the gears could be just scripted, governed by functions that completely ignore any physics. However, the peculiar feature that the prototype is tasked to show is when the Machine is supposed to “jam”. Cannon.js should make this feature possible to render in a simulative way.

Hopefully, these libraries and the JavaScript technology will make the prototype of the Machine work as if it were a real object, just suspended in a virtual world.

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