Chapter 12
Genomics Metaphors and Genetic Determinism

Hub Zwart

The complexities and wonder of how the inanimate chemicals that are our genetic code give rise to the imponderables of the human spirit should keep poets and philosophers inspired for millennia

(Craig J. Venter)

12.1 The Human Genome Project: From *Blueprint* to *Map*

The 20th century has been called the century of the gene (Fox Keller,2000), beginning with the rediscovery of the work of Mendel (in the spring of 1900), coming halfway with the discovery of the structure of DNA (1953) and reaching its 'telos' with the high profile announcement (during the famous White House press conference) that the large scale effort to sequence the human genome was rapidly reaching its conclusion (June 26, 2000).

One of the most tenacious images used to express ideas and expectations related to the human genome has been the 'blueprint' metaphor. In 1999, for example, Francis Collins, director of the Human Genome Project (HGP) indicated that mankind was about to see 'its own blueprint', somewhat earlier than had been originally scheduled (Collins, 1999, p. 28). During the White House press conference in 2000, the sequenced genome was referred to as 'the working *blueprint* of the human race'.[1] The blueprint metaphor became widely used in public debate, moreover, and it was here that it most clearly conveyed its deterministic message. Once we know our blueprint, the metaphor suggests, we will know ourselves. Moreover, others (such as insurance companies or employers) may come to know our blueprints

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(our destinies) as well, and may want to use it to their own advantage. Finally, the idea of a blueprint suggests the possibility of a future mastery over our own nature, over our own destiny as an individual or a species. Through genetic manipulation, a blueprint may be altered in certain directions, by intentionally adding or deleting genes.

Blueprint is also the title of a movie (based on a novel by Charlotte Kerner) featuring Franka Potente as the world-famous pianist and composer Iris Sellin, but also as her daughter Siri. Unwilling to accept her premature decline and death, Iris decides to produce a clone of herself with the help of a genomics expert. In the course of the film, however, the idea of the genome as a blueprint, notably its deterministic connotation, is undermined rather than reinforced, as Siri develops a personality and biography of her own, quite different from that of her mother (as well as from the latter's expectations). In other words, the basic message of both novel and movie is that we cannot meaningfully say that we 'are' our genes or that we are a copy of our genome, or that parents can determine the personalities of their off-spring by means of genomes-as-blueprints.

Interestingly, most of the scientific genomics literature (notably the more recent strain of publications, from 2000 onwards) carries the same message. Quite often, the blueprint metaphor is used to indicate what the human genome is *not*: the human genome is '*not* our blueprint'.[2] Even authors like Collins (1999), who have used the metaphor every now and then, as convenient shorthand so to speak, emphasize that, as such, it is a rather misleading image. Much more adequate, much more in vogue among genomics researchers is the comparison of the human genome with a *landscape*,[3] of the HGP with a grand *expedition* – like the one led by Lewis and Clark in the beginning of the nineteenth century (Collins, 1999, p. 28) – and of the sequenced genome as a *map*.[4] Indeed, the map metaphor is multi-dimensional, it involves multiple layers. It defines the HGP as a large-scale mapping endeavour, funded and coordinated by governmental bodies, supported by heads of state, and directed towards charting (and, as a more or less inevitable consequence, claiming and annexing) unknown territory (Fig. 12.1).

Interestingly, notwithstanding their apparent incompatibility, both metaphors (the blueprint metaphor and the map metaphor) are often used simultaneously, as complementary images as it were. I already referred to Collins' paper where both images are used on one and the same page. This also occurred in the formal addresses during the White House press conference in 2000: while Blair (via satellite) referred to the

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[2] Sulston, 2002/2003, p. 24.

[3] The human genome was officially declared complete (at least in draft form) in February 2001 with the publication of two special issues of *Nature* and *Science*, in which the two rival armies of scientists deigned to summarize the breathtaking landscape of the human genome (Davies, 2001/2002, p. xv); Cf. the comparison of seeing the 'genome landscape' of human chromosome 22 to 'seeing the surface or the landscape of a new planet for the first time' (p. 194).

[4] Robert Cook-Deegan (1994/1995) also compares the HGP to officially ordained and coordinated efforts to survey land and coastal regions, thereby opening up the West. Yet, his favourite comparison is John Wesley Powell's survey of the American West (p. 176).

Fig. 12.1 'A Map of Lewis and Clark's Track, Across the Western Portion of North America from the Mississippi to the Pacific Ocean.' Copied by Samuel Lewis from the original drawing by William Clark. Published in 1814

sequenced genome as 'the working *blueprint* of the human race', Clinton (perhaps on Collins' instigation) preferred to compare it to the Lewis and Clark map. They seem to constitute complimentary images in various ways: the one a simpler and more accessible, but also more or less misleading image, the other a more sophisticated visualisation. Maybe they are even intended to address two different kinds of audiences: the genomics literate and the genomics illiterate. One of the drawbacks of the blueprint metaphor is that it tends to consolidate this demarcation between the masses and the scientifically enlightened elite.

12.2 The Map Metaphor

Before the launch of the HGP, the human genome was regarded as virtually unknown territory in which only a limited number of markers ('genes' involved in a number of mono-genetic health problems) had been identified. The 'wars' (Cook-Deegan, 1994/1995) that marked the preparatory and early phases of the project notably concerned the question *what kind of map* had to be drawn. Should map-making focus on arable, habitable, usable land (the 'genes') or should the map cover all of the genome instead, irrespective of the amount of genes that particular parts of the genome were likely to contain? The latter would involve a comprehensive view of the entire genome, including vast tracks of incomprehensible DNA. On the basis of automated sequencing, the project leadership eventually opted for the latter.For such an endeavour, the Lewis and Clark map offered a historical model.

Meriwether Lewis (1774–1809) was a captain in the U.S. army who became private secretary to US President Thomas Jefferson in 1801. Under the latter's direction, he planned an expedition (sponsored by the U.S. Government) to explore a route through the Western wilderness all the way to the Pacific coast, invit-

ing William Clark to join him.[5] They travelled up the Missouri River through what is now North Dakota and across the Rocky Mountains until they reached the Pacific coast in what is now Oregon, returning home in 1806, after having travelled a total of 8,000 miles (12,800 km). Apparently, both President Clinton and Francis Collins could readily identify themselves, to some extent at least, with President Jefferson and his 'trusted aid' who was asked to lead such a watershed endeavour, culminating in a 'map' of pivotal importance, uncovering (and, by implication, annexing) huge expanses of more or less unknown landscapes. Huge areas were represented systematically on this map, regardless of their potential for future use.

The map image has obvious benefits in comparison to the blueprint image. It is a metaphor that conveys a much less deterministic vision. The physical or geographical characteristics of a particular area or site do not completely determine its future uses or functions, at least not in a truly deterministic fashion. Rather, map-drawing is an activity that makes a whole range of subsequent activities of exploration and exploitation possible. Although it indicates the raw features of a landscape as given, there are various ways to inhabit, cultivate and relate to it. Practices of exploitation and cultivation are not determinalistically *determined* by the map. Moreover, large portions of a landscape are apparently 'useless' (junk), barren remainders of former geological epochs, as is the case with human DNA. At first, habitable areas seem like islands amid a sea of uninhabitable wilderness. Also, map-making marks both the end of an era (exploration) and the beginning of a new one (colonisation) – and this roughly corresponds with the shift from structural genomics (sequencing the genomes of model organisms) to functional genomics (understanding the meaning of this plethora of information).

These characteristics of maps like the one drawn by Lewis and Clark can readily be associated with the HGP as well. The latter also constituted a state sponsored expedition, using established institutes and infrastructures to support it (although in the case of the HGP the role of the U.S. army was played by the N.I.H.). By getting involved, such institutes expanded their realm of action. Once the map is completed, researcher may try to explore the function of genes, like settlers who are drawn to certain areas on the map, but they are bound to discover that a large number of factors are involved in determining the basic features of a particular section of the landscape. Instead of finding mono-causal relationships between single genes and single traits, they will be confronted with multi-factorial and complex relationships between genes and environmental factors. Finally, maps like the one by Lewis and Clark will invite governments to further invest in coordinated research activities as well as in the development of infrastructure. Map-making is the beginning of a process of annexation, colonisation and exploitation.

In other words, map-making is not at all an innocent endeavour devoid of risks. Maps are not innocent tools. They may, for instance, encourage or at least facilitate

[5] See appendix to the Lewis and Clark map.

a gold rush (either a real one or a metaphorical 'gold rush' for genes). Thus, a map may urge policy-makers to take preventive actions in terms of legislation, regulation and surveillance. In other words, genome sequencing as map-making has to be accompanied by programs addressing the Ethical, Societal and Legal Aspects involved – or ELSA genomics – as an endeavour that produces its own kind of map, indicating potentials and risks of future uses in terms of possible societal impact.[6]

Furthermore, it seems as if, as the HGP was making progress, uneasiness with the blueprint metaphor has tended to increase. Initially, programmatic papers describing the HGP and its objectives quite often conveyed a more or less deterministic philosophy. Once the human sequence would be in our hands, it was expected that researchers would have powerful tools at their disposal for discovering genes that were seen as causing a broad range of health problems. Gradually, however, this 'epistemological optimism' became subdued. Apparently, one of the reasons for questioning and eventually dropping the blueprint metaphor has been the remarkably small number of protein-coding genes that have been located on the human genome (Zwart, 2007). Initially, estimates of the number of genes on the human genome tended to vary greatly, ranging from ~ 80,000 to ~ 200,000 genes. Walter Gilbert (1992) suggested that the human genome contained something like 100,000 genes. In 2001, the official estimate of the International Human Genome Sequencing Consortium (IHGSC) was reduced to ~ 31,000 genes and in 2004, in the paper that described and discussed the finished version (build 35), covering 99% of the human genome, a more or less final estimate was given. Apparently, the human genome contains only ~ 22,500 genes (IHGSC, 2004). In 2000, Craig Venter had already concluded that we do not have enough genes for the idea of genetic determinism to be right and Stephen J. Gould (2001) likewise stated that the 'humbling' number of genes implies the death of genetic determinism. The HGP, he argued, had undermined rather than reinforced the 'view of life' from which it started, embodied in what geneticists literally called (admittedly with a sense of whimsy) their 'central dogma': one direction of causal flow from code to message to assembly of substance. According to Gould, 'biomedical research over the past decade has been dominated by a genetic determinist understanding of disease and the discredited doctrine of "one gene, one protein". One thing the human gene map does tell us is that there are ten times as many proteins as genes. Genetic determinism is dead.

In terms of biomedical applications, Huntington's disease, as a mono-genetic health problem, no longer constitutes the model, but rather the exception. The vast majority of human diseases (notably the more common ones) have come to be seen as multi-factorial (involving various genes in interaction with lifestyle and environmental factors). And indeed, even the aetiology of health problems that were formerly seen as 'mono-genetic' prove increasingly complex in comparison to what was initially suggested.

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[6] The map-making metaphor also applies to the so-called 'second' Human Genome Project, namely the Human Diversity Project, led by Luigi Luca Cavalli Sforza and resulting in a 'genetic' geography of mankind. Cf. *The history and geography of human genes* (Cavalli-Sforza, 1994).

12.3 The Blueprint Metaphor and Its Discontents

The shift in terms of basic metaphors from blueprint to map not only has major implications for various issues regarding determinism and reductionism of the type that have been addressed by philosophers of biology for decades, it also affects the agenda for the debate over the societal impact of the HGP and of genomics more generally. Initially, societal issues involved in the HGP tended to be framed in terms of a 'deterministic', single-gene perspective. In their book *Dangerous Diagnostics: Social Power of Biological Information* Dorothy Nelkin and Laurence Tancredi (1989) emphatically highlighted the possible adverse effects of genomics information. They described a rather bleak prospect concerning the societal consequences of the availability of new forms of genetics information. According to these authors, genetic testing was likely to influence life insurance policies and job prospects in such a way that they predicted the emergence of a class of genetic pariahs. Similar concerns are voiced by Paul Billings (1988). But the point of departure of their arguments tends to be a deterministic understanding of genomics. Some individuals apparently carry faulty genes on their genomes and may fall victim to discrimination. Francis Collins himself (like several other prominent genomics researchers) expressed similar concern over 'genetic discrimination', notably in the context of health insurance and employment (Collins, 1999, p. 34; Collins et al., 2003, p. 843). Indeed, even during the 2000 Press Conference, the issue of 'genetic discrimination' was explicitly addressed as a major issue of concern.[7]

Yet, as genomics research continued to evolve, the framing of the societal issues had to be changed significantly. This is reflected in the vicissitudes of the blueprint metaphor as well. Increasingly, it came to be used in order to describe the kind of *misunderstandings* that still prevailed in the public realm concerning genomics. Genetic determinism, symbolised by the blueprint concept, had become a misconception that threatened to affect the quality and adequacy of public understandings of genomics. According to Venter, those who 'base social decisions on genetic reductionism will be ultimately defeated by science', and it was precisely for this reason that he regarded new legislation to forego genetic discrimination of critical importance.[8] In other words, genetic discrimination would not be a consequence

[7]Craig Venter for instance stated that: 'I know from personal discussions with the President over the past several years, and his comments here this morning, that genetic discrimination has been one of his major concerns about the impact of the genomic revolution. While those who will base social decisions on genetic reductionism will be ultimately defeated by science, new laws to protect us from genetic discrimination are critical in order to maximize the medical benefits from genome discoveries'. (http://www.genome.gov/10001356)

[8]I am concerned, as many of you are, that there are some who will want to use this new knowledge as a basis of discrimination. A CNN-Time poll this morning reported that 46% of Americans polled believe that the impact of the Human Genome Project will be negative. We must work together toward higher science literacy and the wise use of our common heritage. I know from personal discussions with the President over the past several years, and his comments here this morning, that genetic discrimination has been one of his major concerns about the impact of the genomic revolution. While those who will base social decisions on genetic reductionism will be ultimately

of genomics research as such, but rather of the lingering influence of the blueprint metaphor, that is: of the fact that employers, insurance companies and others might continue (for some time to come) to adhere to a blueprint-understanding of the genome, although it had become obsolete in scientific circles. According to Robert Cook-Deegan (1994/1995) it should be the basic objective of societal research on genomics to 'recast the debate about genetic determinism' (p. 351). In the early decades of the 20th century, genetics as a science got caught in 'simplistic [i.e. deterministic] interpretations'. Will the same deterministic interpretations continue to dominate public discourse? According to Cook-Deegan, one of the most daunting tasks of the ELSA genomics program will be to change the social framework in which genetics is cast and to take the public debate 'beyond ideologies' towards a richer understanding of the relationship between genome and life (p. 351). The public debate should not repeat historical mistakes premised on genetic determinism. Rather, the extreme complexity of genomics should be its point of departure. 'Caricature' should be replaced with nuance and societal research should provide a richer vocabulary for understanding genetics. This also has consequences for ideas about genetic enhancement and trans-humanism. It no longer seems realistic to believe that we can 'improve' ourselves by adding genes. Whereas traditional biotechnology relied on a deterministic conception (manipulating mono-causal relationships by adding or deleting single genes), genomics urges us to opt for a systemic approach. According to Cook-Deegan, the basic outcome of the HGP is that science has only just begun to understand the complexities of the genome 'landscape'. Once again, the map metaphor seems more adequate than the blueprint metaphor, as a map is something than can be continuously refined and amended through further research.

So far, we have focussed on the map metaphor as it functioned in the context of the public programme. However, the effort to sequence the human genome was actually a competition between two different teams, two different strategies, headed by two highly visible leaders, namely the NIH-based effort under de leadership of Francis Collins and the privately-funded effort under the leadership of Craig Venter. How did the map metaphor function in Venter's case?

12.4 Craig Venter as a Geographer of Life

In the writings of Craig Venter the blueprint metaphor experienced roughly the same vicissitudes as was already indicated above: it was used as well as rejected and as the sequencing efforts progressed, the inadequacies of the blueprint metaphor became more obvious. Interestingly, however, in Venter's case the *map* metaphor became increasingly important *after* his impressive contribution to the human genome sequencing effort had been concluded. Sequencing the human genome was merely a chapter in a biography that encompassed genome sequencing of many other species as well.

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defeated by science, new laws to protect us from genetic discrimination are critical in order to maximize the medical benefits from genome discoveries.

Venter's model expedition, resulting in a different kind of map, was not the Lewis and Clark expedition that served the role of founding narrative for Collins, but rather the expedition that was launched a quarter of a century later (namely in 1831) and that enlisted Charles Darwin as a naturalist: the journey of H.M.S. Beagle around the world. The primary objective of this journey was to conduct a series of hydrographical surveys, a kind of map-making effort in its own right. Due to Darwin's work, however, the significance of the journey shifted from the spatial to the temporal dimension. Its major impact shifted from map-making in the context of oceanography to Darwin's contribution to our understanding of the history and future of life on earth. Venter's Sorcerer II expedition is a global sampling expedition directed towards sequencing the metagenomes of the oceans, i.e. sequencing the genomes of aquatic microbial organisms present in samples of sea water. According to Venter, this effort is bound to have a tremendous impact on our views on evolution as well as on our understanding of global warming. The picture below is taken from an article by Venter's team (Rusch et al., 2007) describing part of the Sorcerer II global ocean sampling expedition as a systematic effort to map microbial life worldwide, a geography of life, an effort to 'explore the incredible diversity of the sea' (Venter, 2007, p. 332) (Fig. 12.2).

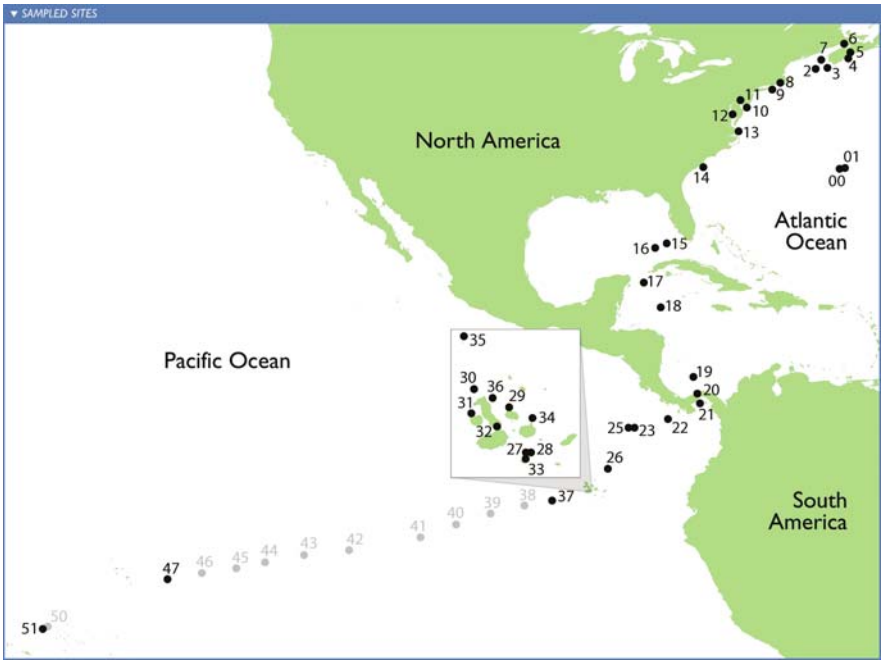

Fig. 12.2 Map of sampling sites. From: Rusch, D. B., Halpern, A. L., Sutton, G., Heidelberg, K. B., Williamson, S., et al. (2007). The Sorcerer II global ocean sampling expedition: Northwest Atlantic through Eastern Tropical Pacific. *PLoS Biology, 5*(3), e77 DOI 10.1371/journal.pbio.0050077

The latter quote is taken from Craig Venter's recently published autobiography *A life decoded* (2007). Its final chapter is devoted to metagenomics: sequencing life on our 'blue [i.e. aquatic] planet'. It invokes a plethora of images connected with exploring and map-making. After the human genome, Venter now became immersed in a geography of life as such. Because we live on land, a terrestrial and even anthropocentric view has dominated our view of life, but the earth is the 'blue planet', aquatic rather than terrestrial. His voyage of exploration amounts to taking snapshots of ocean life. The basic idea is simple: obtain seawater from the ocean's surface at regular distances and capture all the micro-organisms present in it. The focus shifted from genomics (directed towards sequencing the genomes of model organisms) to meta-genomics. 'Rather than focussing on the hunt for one particular type of life', Venter explains to his readers,' we would obtain a snapshot of the microbial diversity of a single drop of seawater – a genome of the ocean itself' (p. 343). This meant opening up previously unknown realms for human exploration and understanding: 'We had opened to doors to a world that has been mostly unknown to modern science. From the sunlit surface to the darkest submarine canyons stretches an ocean of life that is beyond human imagination' (p. 344). Thus, the team discovered tens of thousands of new species and something like 1.3 million new genes in about 200 litres of surface seawater.

Although sequencing in Venter's case still amounts to a map-making effort, mapping the earth is a different kind of venture, involving a different set of images and metaphors, than mapping aquatic regions, let alone the wide expanses of the ocean. Images of mapping the earth are connected with claiming and annexing unknown territories on behalf of governments and administrations. Map-making is a technique involved in practices of power, directed towards establishing legitimate forms of governance over novel areas, notably at a time when political hegemony is far from stable. In other words, mapping the earth is a practice that is part of strategies of colonisation and annexation, establishing firm governance on *terra firma*. It is an effort to transform the diffuse and unknown into something discrete and accessible, and therefore governable.

Aquatic metaphors are different. The sea has always been associated with freedom of movement, with migrating beyond the spheres of action of established rulers. In Venter's biography, science and sailing are intimately connected. Whereas Collins identified himself as a 'trusted aid' in service of a governmental programme, Venter's work has always had a rather different moral profile, that of embarking and setting sail to places where one is left to one's own devices and 'where there is still an ocean of great science left . . . to explore' (p. 357), discovering new worlds, breaking away from entrenched positions. In Venter's view, science is an endeavour that takes us 'far from shore into unknown waters' (idem). It defies, rather than reinforces, political authority.[9]

[9] This difference is also indicated by the icons Collins and Venter preferably used in self-presentations: Collins seated on his motorbike or playing *country* music on his acoustic guitar, and Venter on his sailing yacht – icons that symbolise terrestrial and aquatic forms of mobility.

On further reflection, Venter choice of Darwin's voyage as a model for his own endeavour seems less than optimal. A far better candidate to serve as a paradigm or archetype for the Sorcerer II expedition would have been Captain Nemo's journey on board the *Nautilus*, to which Jules Verne devoted his masterwork *Twenty-thousand leagues under the sea*. Nemo's venture was a privately funded endeavour, far beyond the sway of nation states, to chart the oceans, notably oceanic life, of which virtually nothing was known to established academics at that time. Like the Sorcerer II, the *Nautilus* was basically a floating research station, a self-sufficient observatory that placed oceanography (notably the survey of oceanic life forms) on a radically new scientific footing. Moreover, as in Venter's case, it was a voyage that defied political authority and took place far outside the reach of official science funding and science administration, although, unlike the secluded Nemo, Venter continued to communicate with terrestrial public and academic life through his scientific papers in established peer-reviewed journals and his autobiography.

12.5 Genres of Imagination: Novels as Research Tools

Midway between academic scientific writing and societal debate there is an intermediate level of discourse, a migratory zone so to speak, where the cultural impact of the sciences in general, but also more specifically of genomics and the HGP in particular, is being discussed, and where images and metaphors are being adapted and refined, altered and reinforced, namely the genres of imagination (novels, plays, movies and the like). These sources explicitly reflect on, or even anticipate, major scientific breakthroughs while considering their meaning for society. They tend to have a significant impact on societal debate, notably on the metaphoric level. To a considerable extent, the images that are used to frame public debate over biotechnology and the life sciences are coming from novels (*Frankenstein*, *Brave New World*, etc.). Therefore, Gregory Benford (2001) argued in *Nature* that scientists should try to learn something from the 'what if' mentality of these literary science authors, notably when it comes to assessing the public and societal impact of their work. They should pay more attention to laboratory literature and science fiction. Public ideas concerning science 'usually begin in literature and migrate to the visual media' from there. In order to understand or even influence the ways in which research is perceived, scientists 'would do well to pay attention to the storytellers and dreamers'. Science fiction is our biggest mirror, reflecting the literary imagery of science. Since Mary Shelley's *Frankenstein*, the prospects that science opens have played a significant role in our culture' (p. 399). Indeed, these writers work out the possible societal consequences of innovations long before they arrive in common culture:' When Dolly the sheep made cloning a media event, the scientists involved did not notice that science fiction had discussed the issue extensively decades before' (idem).

Of particular interest in this respect is a specific sub-genre called 'laboratory literature' or simply *lab lit* (Rohn,2006).[10] Strictly speaking, lab lit is *not* 'science fiction', although the distinction may often be a fluid one. Rather, laboratory literature depicts scientists in more or less realistic settings and portrays fairly realistic scientific practices or concepts, typically taking place in a contemporary – as opposed to a distant, speculative or future – world. Its basic aim is to capture and assess in a literary manner various research practices currently emerging in laboratories. Moreover, through extrapolation, this type of literature sets out to explore what the consequences of certain developments may be for culture and society. To the extent that it manages to do so, it must be regarded as a valuable source of information and inspiration for science research. It can be helpful when it comes to addressing questions such as the general profile of genomics, the view of nature it conveys and the societal consequences it entails. In short, novels belonging to this genre may be regarded as scenario studies, as research tools.

The idea of the novel as research tool is not new. The French novelist Emile Zola (1880/1923) regarded the novel as a 'literary experiment' (in the literal, i.e. *scientific* sense of the term). Zola was an enthusiastic reader of Claude Bernard's famous textbook *Introduction to the study of experimental medicine* (1865/1966). Bernard is generally regarded not only as one of the heroes of biomedicine, but also as one of the 'champions' of vivisection, subjecting large numbers of animals (notably rabbits and dogs) to painful and usually fatal experiments. Although as a youth he had tried his hand at playwriting, he decided to abstain from writing belles-lettres completely and to devote himself to science instead. He called his method 'experimentation by destruction' (p. 37). According to Bernard, the logic of experimentation basically consists in *destroying* or removing a particular part of the animal's body (such as an organ, a tube, a nerve, etc.), in order to *observe* the effects of this destruction in the organism. In this manner he was able, for example, to discover the function of the liver. For centuries anatomists had been unable to understand the role of this large mysterious organ, but Bernard showed that an experimental approach could solve the riddle. According to Bernard, the experimental scientists deliberately act upon nature, damage nature, in order to observe the effects of their own doing. They artificially produce the phenomenon they want to study. As he states in his *Introduction*, the hand of the experimenter must actively intervene in order to allow the phenomenon under study to appear (p. 27). Indeed, the success of experimental work greatly depends on the technical skills and technical devices scientists have at their disposal to manipulate the organism.

In one of his essays, Emile Zola argues that the above applies to novel-writing as well, to such an extent that, if one simply replaces the word 'researcher' by 'novelist', one will end up with a perfect description of what novel-writing basically amounts to. The author drastically intervenes in the lives of his characters, exposes them to a variety of carefully selected 'conditions', in order to study and record the effects of these conditions as acutely as possible. 'Naturalistic' or

[10] http://www.lablit.com.

'experimental'[11] novels constitute a complimentary discourse to laboratory research, testing and extrapolating laboratory findings under real life conditions. In Zola's view, novels represent a test bed where physiological and psychological views borrowed from scientific accounts can be further elaborated. The concept of the experimental novel, he claims, puts the art of novel-writing on a scientific footing, more or less as Bernard had done with the art of medicine. Rather than describing the world as it presents itself to us, the experimental novelist actively alters the conditions in order to expose his characters to specific circumstances and events. Subsequently, like a real experimenter, he carefully studies their responses. As Zola sees it, the naturalistic novel really *is* an experiment, in a genuinely scientific (Bernardian) sense of the term.The novel is a laboratory, where social phenomena may be analysed systematically. Naturalistic novels must display the same measure of detachment and precision as scientific research reports.

12.6 Genomics Novels

A prominent example of contemporary laboratory literature, but at the same time of experimental novels, is the work of Michael Crichton (1942–2008). In his novels Crichton explicitly claims to address important dimensions and dynamics of contemporary cutting-edge research, including the impact of ICT, the role of public pressure groups or the influence of commercialisation, notably in the field of genomics. Novels such as *Jurassic Park* (1991) or *Next* (2006) explicitly try to explore how genomics as a research field is evolving and what its possible societal and cultural impacts may be. These novels claim to analyse and critically assess the transformations in knowledge production that are taking place. Moreover, they are structured as literary experiments. They stage a series of extrapolations of laboratory developments by introducing genomics into various real-life practices. In other words, his novels may be regarded as literary scenario-studies, literary counterparts to ongoing research efforts in genomics. They try to flesh out, by way of literary experimentation, the epistemological and societal consequences of genomics as cutting-edge science. Therefore, besides revivifying the dormant archetypical images that structure public imagination (such as the monster archetype), his novels also have the explicit aim to contribute to our understanding of how science works, and how particular research practices may interact with their cultural and societal environments.

Genomics research inspired other examples of laboratory literature as well, such as, for example, Michel Houellebecq's *Elementary Particles*, published in 1998.

[11] In the context of literary writing, the term 'experimental novel' may be confusing. Usually, it refers to texts that try to go beyond established or standardized patterns of literary discourse – something like 'beyond method' or *anything goes*. Zola, of course, had something completely different in mind. He was rather thinking of a very *methodical* type of novel.

This novel was based on the idea that the human genetic code can be represented in the form of a mathematical algorithm, thus opening up avenues for artificial reproduction and genetic enhancement, culminating in the production of a new type of human being. What the revolutions of the 1960s (in terms of sexuality, drugs and politics) failed to achieve (namely allowing mankind to take a dramatic leap into a brave new world of human freedom and happiness) will be made possible by genomics. There is some irony in this line of reasoning, of course. What Houellebecq actually seems to be suggesting is that, apparently, the genomics revolution is hailed with the same amount of naïveté as the sexual, political and psychedelic revolutions have been in the course of the 20th century. Eventually, the genetic deterministic presuppositions of the scenario depicted will prove difficult to sustain. Human genetics will be too complex for transhumanism to become reality, at least for the coming decades.

Initially, like *Elementary particles*, Michael Crichton's novel *Jurassic Park* (1990/1991) also seems to presuppose and reinforce a genetic deterministic understanding of life. Eventually, however, the novel rather criticizes a deterministic way of viewing living beings – albeit with the help of literary techniques. Thus, it reflects the same dynamics that is recognisable in the HGP as well. HGP and *Jurassic Park* stand out as complimentary phenomena.

The storyline is well-known: a company called InGen develops a genetic engineering facility on an island in a remote and obscure Central American area with no regulations. A team of prominent researchers is hired to set up a theme park in a resort – a private Jurassic zoo of huge dimensions. They achieve this by remaking Jurassic dinosaurs with the help of supercomputers using paleo-DNA (extracted from blood preserved within mosquitoes entombed in fossil amber). Thus, a number of flagship species of Jurassic palaeontology (whose ecosystems have vanished) are revivified and re-introduced into an environment as 'Jurassic' as possible: an uninhabited tropical forest area. Computational biology is called in to fill in the gaps in the animals' reconstructed genomes. Dinosaurs become experimental animals and palaeontology itself, the study of extinct life, is transformed overnight into an experimental discipline. Excavations are no longer needed.

When Alan Grant, an outstanding palaeontologist, is confronted with the revivified versions of his favourite organisms, he immediately realises the epistemological significance of this event. Palaeontological quandaries that had occupied his research community for years, such as the issue of whether dinosaurs had been warm-blooded or cold-blooded animals, whether they cared for their young and whether they were fast or slow moving, were now easily resolved by merely looking at these 'surprisingly active' organisms: 'Grant's field of study was going to change instantly. The palaeontological study of dinosaurs was finished. The whole enterprise – the museum halls with their giant skeletons and flocks of echoing school children, the university laboratories with their bone trays, the research papers, the journals – all of it was going to end' (Crichton, 1990/1991, p. 84). Meanwhile, the revivification of vanished life forms, based on a reconstruction of their genomes, is

less absurd than it may appear at first glance. The idea has inspired a number of serious research efforts.[12]

The project's fatal flaw, from the very outset, is genetic determinism and reductionism: the idea that organisms can be genetically manipulated effectively by adding or deleting single genes and that in such a way the trial can become predictable, controllable and manageable. Notably, a gene has been inserted so that the animals will be unable to manufacture the amino acid lysine themselves. It has to be administered to them and for that reason they are supposed to be unable to survive in the outside world. Thus, they cannot escape from the sway of genomics science. Yet, in Crichton's narrative, the animals quickly develop other means to satisfy their desire for lysine. The dinosaurs manage to escape from the resort. Life will find a way, as one of the main characters, complexity theorist Ian Malcolm formulates it, in order to survive, to disseminate, to spread. Life will continuously evolve new strategies to take care of itself (p. 369). It will defy containment. The Jurassic animals were supposed never to mix with the ecosystems of the contemporary world, but such isolation proved impossible: 'What we call "nature" is in fact a complex system of far greater subtlety than we are willing to accept' (p. 91). Thus, notwithstanding its apparent determinism, the novel's basic message is that the complexities of life cannot be adequately addressed within the confines of this outdated research philosophy. *Jurassic Park* not only coincides with, but also mirrors the vicissitudes of the HGP. The morale is that a deterministic understanding of life fails to appreciate the flexibilities of living beings, notably their capacity to develop 'emergent behaviour', in interaction with their natural and technological environments. *Jurassic* Park is an entertaining novel, but at the same time it intends to contribute to on-going debates on the profile and impact of genomics science.

In 2006, Crichton published his latest novel *Next*, once again devoted to genomics. Yet, whereas *Jurassic Park* (as well as its sequel *The lost world*) are devoted to sequencing, reconstructing and revivifying the genomes of (extinct) animals, *Next* analyses the impact of genomics in the biomedical sphere, i.e. its consequences for human life (health, labour, sexuality, family life). Therefore, the final section of this paper will be devoted to the question to what extent his latest novel allows us to address the societal implications of genomics research in a post-reductionistic fashion.

[12] Although the bringing back to life of dinosaurs may seem rather improbable and farfetched, the improbability of such an endeavour decreases as the species is closer (geologically speaking) to the present. Mammoth DNA, excavated in Siberian permafrost, or the genome of the Siberian tiger may (from a purely technical point of view at least) prove less difficult to reproduce and clone. In other words, while Jurassic Park may seem somewhat too ambitious, *Pleistocene Park* may prove less futuristic. The idea that in the near future revivified mammoths once again will roam the sub-Arctic tundras and ice fields cannot be discarded as completely absurd.

12.7 Next

At first sight, *Next* is a somewhat confusing novel.[13] Like a genome, it picks up bits and pieces of information as it evolves.[14] Apparently, it is set at various levels. On the surface, it seems to take the logic of genetic determinism to its very extreme, to the point where it becomes utterly absurd.Stories about gene hunting (sociability gene, novelty-seeking gene, infidelity gene, etc.), about transgenic chimpanzees and parrots who can reason and talk, about an ambulance chasing the daughter and grandson of a man from whose tissue UCLA developed a profitable cell line, must be regarded as caricature or persiflage on the basis of exaggeration. Apparently, Crichton seems to argue, this is the way in which the illiterate (and this notably includes lawyers, patent attorneys and judges) tend to view genomics.[15] Bizarre and at times soap-like stories are intersected, however, with reflections on what genomics (notably the HGP) really amounts to. In this manner, *Next* apparently has the intention of making visible the enormous tension between the kinds of insights genomics research is actually producing and the way they are represented in the public realm.

A rather important element in Crichton's novel is gene hunting. A number of 'genes for' play a crucial role in the novel, genes that supposedly determine behavioural characteristics, not only the obvious ones (such as genes for intelligence, alcoholism or sexual orientation) but also the sociability gene, the novelty-seeking gene, the maturity gene and the infidelity gene. The most prominent gene hunter in the book is Dr. Robert Bellarmino, head of the National Institute of Health (NIH), top scientist but also devout Christian, politically skilled and media savvy[16] who, as a referee, systematically rejects applications for funding by rival teams, who deprives his favourite post-doc of the latter's first-authorship, and whose research on the novelty seeking gene incites him to visit amusement parks in order to collect genetic materials. As a consequence of Bellarmino's publications (fifty papers a year), lawyers are considering the option to use screening for the novelty-seeking gene as a mitigating circumstance on behalf of clients who happen to engage in risky lifestyles, or to subject former partners to genetic screening in the context of custody cases. Treatment of drug addicts with sprays containing an experimental virus that carries the maturity gene will solve their drug problem, but also causes premature ageing.

In most of these cases, there is some connection with serious research. In 1996, for example, a research group led by Dean Hamer confirmed that variation in the

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[13] Cf. 'Crichton tries to address every aspect of the biotechnology craze at once, giving the book too many simultaneous plotlines to follow' (Goldman,2007, p. 819).

[14] 'I wanted [the book] to be in a way analogous to the genome. The genome accumulates bits and pieces of genetic material over time. It gets viruses. They get incorporated. So I started incorporating a fair number of things … true stories that I just stick in the book.' [http://www.michaelcrichton.net/charlierose-021907.pdf]

[15] 'The courts are incompetent … because they are technically illiterate' (p. 56).

[16] My impression is that Bellarmino represents a mixture of Craig Venter and Francis Collins.

length of the gene for the dopamine D4 receptor correlated with 'novelty seeking', i.e. extravert and thrill-seeking behaviour (Benjamin et al.,1996; Cf. Hamer and Copeland,1998). Yet, the small print in Hamer's *Nature Genetics* study was overlooked: 'this was far from the gene for bungee jumping, as some newspapers reported' (Davies 2001/2002, p. 233; Cf. Paterson, Sunohara, & Kennedy,1999). Likewise, research has been published on the sociability gene, but it concerns solitary versus group feeding in C. elegans[17] and it is far from evident how such a finding, if at all valid, could be extrapolated to the intricacies of human behaviour. In Crichton's book, prominent researchers like Bellarmino are portrayed as people who, in a rather cynical manner, 'take advantage of the public's lack of knowledge about how genes actually operate. No single gene controls any behavioural trait' (p. 158). He represents a new generation of highly visible and highly influential scientists, people who 'sit on the boards of private companies, and are in a race to identify genes they can patent for their own profit' (idem).

As is the case in *Jurassic Park*, these gene hunters, as well as the simplifying view on genomics they convey, are counterpointed by a number of (usually much less visible and affluent) critics, such as professor William Garfield of the University of Minnesota who, lecturing before a group of congressmen, claims that 'despite what you hear, nobody has ever proven a single gene causes a single human behavioural trait... The interaction of genes and environment is just too complex' (p. 211). Garfield argues that publications on new 'genes for' are often misrepresented: they refer to statistical association, not at all to causal relationships. There is, for instance, no single gene that accounts for alcoholism. The public readily believes that genes cause behaviour, but the actual relationship between genes and environment is very complicated. Scientists do not have a good understanding of how genes work. In fact, 'there is no general agreement on what a gene is... [Among scientists] there is no single agreed-upon definition of what a gene is' (p. 212).[18]

In his briefing, Garfield also mentions how startled scientists initially were to find such a small number of protein-coding genes on the human genome. 'After all, a lowly earthworm has 20,000 genes. How, then, could you explain the huge difference in complexity between the two? That problem vanished as scientists began to study the interactions among genes [and began to move into] "epigenic studies", which look at exactly how genes interact with the environment to produce the individual that we see' (p. 213). Yet, this briefing more or less stands out as an intellectual intermezzo, comparable to the monologues of Ian Malcolm in *Jurassic Park* and *The Lost World*. As a rule, Crichton prefers to rely on his strategy of extrapolation *ad absurdum*, fleshing out what genetic determinism may lead to (if it is really taken seriously) in various real-life settings involving love, family life and divorce.

A number of other normative issues are addressed as well, for example issues having to do with scientific authorship and the various threats commercialisation represents to the ethos of science through gene patenting. Because of these

[17] On the 'sociability gene' see for instance. *Nature, 395* (24 September 1998), p. 327.

[18] Cf. for example Dupré (2004) for a philosophical version of this debate.

developments, research findings are increasingly disseminated through press conferences and press releases, rather than through academic journals.[19] According to Crichton, university groups are increasingly reluctant to publish their work in the conventional manner. Moreover, even prominent academic journals can no longer be trusted: 'Remember that the journal *Science*is a big enterprise – 115 people work on that magazine. Yet, gross instances of fraud, including photographs altered with Adobe Photoshop, often go undetected' (p. 62). Indeed, 'even Francis Collins, the head of NIH's Human Genome Project, was listed as co-author on five faked papers that had to be withdrawn' (p. 62), which, in fact, is true. According to Crichton, three million researchers are working in this field and this implies that the stakes are high. Traditional scholarly mechanisms can no longer be trusted to effectively cope with the consequences of commercialisation. And indeed, in prominent journals such as *Science*, embarrassing retractions (because of fraud or premature and unconfirmed results) have become part of daily practice.

Commercialisation not only affects the research community, but the outside world as well. Patients are asked to sign informed consent forms to sell their tissue, and if successful pharmaceuticals are developed on the basis of the resulting cell-lines, this may lead to more or less absurd disputes over property rights. Or body materials are obtained illegally from deceased persons. Young women (including Bellarmino's daughter) are enticed to inject drugs and hormones into their bodies in order to stimulate their ovaries and sell their eggs – perhaps a reference to the case of Woo-Suk Hwang, who is actually mentioned several times in Crichton's novel – although, in this case, the young women involved receive money which they use to buy breast implants. Although in principle some of these issues are real enough, they clearly suffer from Crichton's strategy of exaggeration (Goldman, 2007).

Crichton's ultimate target, however, is gene patenting, the heart of the matter, and a practice he considers to be absurd. Moreover, it is here that normative concerns over commercialisation most clearly converge with epistemological issues (the reductionism-versus-complexity debate). According to Crichton, our growing awareness of the complex relationships between genes and disease, and between genes and behaviour, renders the very idea of patenting genes absurd. Not only because genes are facts of nature rather than inventions, but also because one-to-one relationships between genes and function are the exception rather than the rule. Therefore, genomics research has made ideas about owning genes and manipulating genomes (notably in the context of behavioural transformation) quite implausible. Gene patenting, and the philosophy of genetic determinism that inspired and legitimised this practice, is at the root of most of the soap-like absurdities Crichton stages in his novel. Mastery over (human) nature has – at least – two meanings: ownership (of genes) and manipulation (by adding or deleting single genes). Both are undermined by our growing awareness of the human genome's complexities. Yet, in

[19]The 2000 press conference, rather premature and hastily contrived (Davies, 2001/2002, p. xv) was, in fact, an example of this policy.

order to really bring this to the fore, Crichton should perhaps have written a novel containing a somewhat smaller amount of farce. In that respect, *Next* does not compare favourably with *Jurassic Park*. Yet, it serves its purpose as a first literary effort to map and chart the complex and emerging societal landscape of genomics.

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