“ Self-Assembly, Self-Organization:A Philosophical Perspective on a Major Challenge of Nanotechnology

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Put the different parts of a car in a big box, and shake the whole, will you get a car? This image is often used to express what self-assembly can achieve.[1] Spontaneous arrangements of small building blocks in ordered patterns or structures are ubiquitous in living systems, and they are crucial for designing at the nanoscale, where human hands and tools are helpless. Self-assembly is extremely advantageous from a technological point of view because it is a spontaneous and reversible process with little or no waste and a wide domain of applications ranging from nucleation of inorganic particles, formation of vesicles, monolayers, supramolecules, etc.

Over the past decades, self-assembly has attracted a lot of research attention and transformed the relations between chemistry, materials science and biology. A bibliometric survey of the occurrences of the term “self-assembly” in comprehensive data-bases (the ISI: Science Citation Index/SCI and Social Science Citation Index/SSCI) by Sabine Maasden and Mario Kaiser reveals a spectacular increase over the past twenty years.[2] According to their survey about 10% of the papers devoted to nanotechnology address the concept of self-assembly. Among them a small portion (about 3%) are dealing with self-organization (176 over an amount of 5741 papers in the year 2005).

Table 1: Self-Assembly occurrences in SCI & SSCI

1990	1995	2000	2005
86	**807**	**2444**	**5741**

A wide spectrum of self-assembly techniques have been developed and described in the technical literature.[3] The car metaphor is rather used in semi-popular publications. It is meant to emphasize the novelty of nanotechnology and the radical break with conventional top down fabrication techniques. On the other hand, it conveys a kind of magic power to

[1] Drexler, *Engines of Creation*, p. 2 ; Richard Jones rather used the metaphor of the iigsaw puzzle (Jones, 2004, p. 91-93)
[2] Maasden (2006)
[3] see Whitesides and Boncheva (2002), Zhang Shuguang (2003), *MRS Bulletin*, 31, January 2006,

nanoscientists.[4] The access to the nanoscale also triggers the ambition to create artificial cells and to unveil the mystery of the origin of life.

From a historical perspective, self-assembly strikes as a new episode in a long tradition of Faustian ambitions to rival with life. Paracelsus already claimed that alchemists could create an artificial human being, a homonculus in a test-tube.[5] Later on nineteenth-century chemists spread the legend that the synthesis of urea by Friedrich Wöhler destroyed the metaphysical belief in the existence of a vital force since chemistry was able to synthesize substances so far made only by living organisms.[6] It was not difficult however for physiologists such as Claude Bernard to ridicule their claims by pointing to the huge difference between their laboratory processes and nature's processes. Chemists could certainly synthesize the products of life but could not imitate the ways of nature in their vessels and furnaces.[7] Thus their anti-metaphysical claim proceeded from two confusions: between "organic" and "organized" and between product and process. However today chemists seem to be in a better position to silence Bernard's objection. Self-assembly seems to open a path for emulating nature's processes. Are we going to witness a new episode of the endless fight between vitalism and reductionism? Will history repeat itself? And to plagiarize Marx's famous remark, while putting it upside down: shall we say that the first time it was a comedy and that the second time it could be a tragedy?

Over the past decades, the emergence of nanotechnology has been fuelled by visions of the future, both utopian and anti-utopian. The main motif of apocalyptic scenarios is the loss of control of devices implemented in nano-objects especially those generated by the convergence of Nano, Bio, Info and Cognitive sciences (NBIC). Jean-Pierre Dupuy has argued that cognitive science provides the guidelines for the NBIC convergence and orientates the program towards the loss of control. [8] Self-assembly being a spontaneous process also raises the issue of control. Indeed there is no real danger of machines running amok, or of self-replicating machines. However self-assembly is clearly a process of construction "in which humans are not actively involved, in which atoms, molecules, aggregates of molecules and components arrange themselves into ordered, functioning entities without human intervention".[9] In a long duration of the history of technology, self-assembly strikes as a step further in the process of delegation of human tasks to matter. After the delegation of a number of mechanical or logical operations to machines, the time has come to delegate the construction of machines itself to matter. What can be the impact of this "next step" on the responsibility of designers?

I Three distinctive strategies

[4] Actually some scientists like to play magics. In a recentbig international chemistry conference, David Leigh from Edimburgh performed magic tricks while presenting the results of his work on self-assembly.

[5] See William R. Newman, *Promethean Ambitions: Alchemy and the Quest to Perfect Nature*, Chicago, university of Chicago Press, 2004.

[6] Marcelin Berthelot : *La synthèse chimique* (1860)conclusion in 8° édition Paris, Alcan, 1897), p.265-77. On the urea synthesis legend see Brooke, J.H. , « Wöhler's Urea and its Vital Force—A Verdict from the Chemists." *Ambix* 15 (1968):84-114. P. Ramberg « The Death of Vitalism and the Birth of Organic Chemistry : Wölher's Urea Synthesis and the Disciplinary Identity of Chemistry », *Ambix*, 47 (2000) : 170-195
Brooke, J.H., « Organic Synthesis and the Unification of Chemistry – A Reappraisal», Brtish Journal for the History of Science, 4 (1973): 362-392.

[7] Claude Bernard : Sixième Leçon in *Leçons sur les phénomènes de la vie communs aux animaux et aux végétaux* 1878, réédition Paris, Vrin 1966 p 202-229.

[8] Dupuy 2004

[9] Whitesides, 1995.

The purpose of this section is not to survey the various strategies of self-assembly at the interface between nanotechnology and biology, which are described in today scientific literature. Rather I try to distinguish various trends of research using self-assembly, to make a kind of typology. Although the three categories here distinguished may overlap in practice, they deeply differ on the basis of their philosophical assumptions.

- 1 – Using the building blocks of living systems for making devices and machines is the strategy that can be named hybridization.

-2- Biomimetics is making artefacts mimicking nature

3- Integration is a kind of composite of the two previous strategies. .

I do not claim that this tentative categorization does justice to the entire field. The three strategies here described rest on the assumption that artifacts and natural systems share some features and often use the machine metaphor to describe living systems. But the metaphor works in two different ways. Either technological vocabulary is applied to living organisms and describes them as machines or organic metaphors are used to describe our devices and machines. In the 1970s, the French philosopher Georges Canguilhem noticed that the analogy between organism and machines always works one way: organisms being described in technological terms.[10] But what would happen if technology were described in biological terms? If machines behave like organisms and gradually become part of the living world?

Strategy N°1 Hybridization

An obvious way to self-assemble the parts of our machines is to take advantage of the exquisite structures and devices selected by biological evolution. For instance, using biology to build nanoelectronic circuits that assemble without human manipulation. When Erez Braun, a biophysicist from Technion at Haïfa announced that he used the complementarity of DNA strands for making nanotransistors, the news was widely reported.[11] Now it is current routine practice in the laboratory waiting for applications at industrial scale.

The designer of such machines borrow a specific material or device "invented" by biological evolution regardless of its specific environment. Indeed traditional technologies have been doing that for centuries. They used to extract resources such as wood, bone, or skin and process them to make a variety of artifacts, Similarly nanotechnology extracts a number of small units as close as possible to the building blocks of living systems (DNA, bacteria,..) in order to build artifacts from bottom-up.

This strategy requires that the living cell be viewed as a collection of machines operating together. "Molecular machine" is a fashionable expression. It is currently used both by molecular biologists who describe DNA, RNA, enzymes, proteins as nanomachines and by materials chemists who are building molecular motors or rotors. Living systems are viewed as molecular manufactures and the analogy is often used as a proof that we can make it. But there is little chance that we can emulate nature, who spent billions of years for designing and perfecting high-performance structures capable of sustaining life. It seems more reasonable to start from the building blocks provided by nature - whether they be proteins, bacteria, micelles or colloids - in order to achieve our own goals. Steven Boxer, a chemist from Stanford who uses proteins as transistors in electronic circuits, thus describes his strategy: "We've decided that since we can't beat them (biomolecular systems), we should join

[10] Canguilhem, 1971

[11] Keren K, Berman R S., Buchstab E., Sivan U., and Braun E. (2003)

them".[12] "Joining" may not be the most appropriate term for two reasons: i) biomolecular systems have to be decomposed in a number of elementary units, redefined as functionalities, and abstracted from their own environment; ii) they have to be processed and modified through genetic engineering to perform specific tasks in an artificial environment. To consider such uses as a form of partnership ("join") you have to consider that biological systems are fully and adequately described in terms of a collection of independent devices that can be abstracted from their environment and re-used in other environments.
In my view this strategy is more adequately depicted as appropriation of biological items in the dual sense of the term (at least in French): i) they are processed through various techniques (recombination, gene modification, …) in order to be adjusted and adapted to human purposes; ii) they become our intellectual property and can consequently be patented.

Further analysis of the model of machines underlying this strategy points to a number of characteristic features..In fact, the analogy between nature and artifacts is self-reinforcing. The more machines try to resemble living organisms, the more nature is artificialized. However, as shown from the chart below, molecular biologists do not care for shaping a consistent metaphor. Rather they pick up images from a variety of technologies – mechanical engineering, electrical circuitry, information technology…. A living cell looks more like a warehouse or a garage, than like a modern manufacture.

Table 2 What do they have in common? Machines and molecular machines
(From Zhang , 2003, p. 1174)

Machines	**Molecular machines**
Vehicles	Hemoglobin
Assembly lines	Ribosomes
Motors, generators	ATP synthases
Train tracks	Actin filament network
Train controlling center	Centrosome
Digital databases	Nucleosomes
Copy machines	Polymerases
Chain couplers	Ligases
Bulldozer, destroyer	Proteases, porteosomes
Mail sorting machines	Protein sorting mechanisms
Electric fences	Membranes
Gates, keys, passes	Ion channels
Internet nodes	Neuron synapses

More importantly the cell seems to be a collection of independent parts, each of them designed for performing a specific task. In this respect the cell machinery is a very classical machine, such as clocks. In classical or "Cartesian" machines, each individual component is assigned a definite function.[13] Each functional part is independent from the others and has to be assembled together by a specific tool. For instance, Drexler's universal assemblers, modelled on ribosomes, pick and place atoms to assemble them. In this model of machine where each task is correlated with one component, self-assembly becomes a self-contradictory notion. For the machine to be ideal, assembly has to be a functionality belonging to an

[12] Steven Boxer quoted in "Exploiting the Nanotechnology of Life", *Science*, 254, 29 November 1991, p. 1308-09.
[13] Bensaude-Vincent, Guchet (2006)

individual unit rather than a property of the whole. All spontaneous tendency to self-assemble, to stick together is an obstacle.
The Cartesian paradigm underlies a new emerging discipline at the crossroad between nanotechnology and biology. Synthetic biology develops a symmetric strategy of hybridization through the application of engineering approach to biology.[14] The purpose is to break down a biological process into its elements (just as nineteenth-century engineers divided complex processes into “unit operations”). Pieces of DNA are thus redefined as operational units. Then the elements will be assembled together to make a module (for instance, oscillator or switch). The ultimate goal is to make a library of independent and interchangeable parts (“Registry of Standard Biological Parts”) that can be used to perform a specific function everywhere. Right now it looks like an unrealistic program because it is difficult and expensive to collect the biological parts. However as biotech suppliers are proliferating, the expectation of synthetic biologists is that within a few years cheap sequences will be available in department stores of biological parts. The program may be feasible but it will presumably stumble on a major obstacle, the collective behaviors of biological units. [15] In brief, there is no place for any function that is not assignable to a specific unit. If self-assembly is an obstacle rather than a principle of design, it is because it is a collective behavior in addition to being a spontaneous behavior.

Strategy 2: Biomimetics

An alternative strategy is to mimic nature. Even before the nano-tsunami, self-assembly has prompted collaborations between materials scientists and biologists. [16] Materials scientists who turned their attention to natural composites such as wood, bone, muscles, or natural fibers such as spider silk were fascinated by nature’s multifunctional structures and efficient processes. For Mekmet Sarikaya et Olhan Aksai *“ biomimetics is the study of biological structures, their function, and their synthetic pathways, in order to stimulate and develop these ideas into synthetic systems similar to those found in biological systems. “*[17]
The phrase “synthetic systems” suggests that the machine metaphor no longer guides the interpretation of self-assembly and that a more systemic approach prevails.

In fact, in the case of self-assembly mimicking biology cannot be just copying a model. Mimicking biology never meant duplicating the original in all its details or faking it, as could be the case with fine arts copies. Even when materials scientists mimic marine shells for making strong composites, or lotus leaves for making non-wetting glass, they do not make indistinguishable copies. They usually select essential aspects of biomaterials. Yet generally their model is less a living system than a local pattern or device whose performances are interesting for engineers.
When it comes to mimicking processes such as self-assembly, then the laboratory cannot exactly copy the model. Chemists usually operate at high temperatures, in high vacuum and

[14] *Nature* volume 438 24 November 2005 417-18
[15] For instance a team from Berkeley tried to design a new system of communication between cells using interlocking cell circuits rather than relying on simple gene circuits built in single cells. The team exploited a natural method used by bacteria : they conjugate two bacterias by connecting their respective cell walls using a structure called a papilus. The group managed to trigger the conjugation response with synthetic circuits. Alas the bacteria were so eager to join up that they made huge bunches and it was hard to separate them. They can go but they can’t stop ! reported in *Nature* 438 24 November 2005 417-18)

[16] Sarikaya & Aksay 1995, Bensaude-Vincent, Arribart & al., 2002.
[17] Sarikaya et Aksay eds, *Biomimetics : Design and processing of Materials*, AIP Press (Woodbury, 1995) p.xi

with organic solvents, while nature operates at room temperature, in rather messy and aqueous environments. Nature provides inspiration rather than models.[18]

Whereas designers trying to replicate a model have to acquire an in depth knowledege of its fine-grained structure and to look at details through the eyes of a botanists, by contrast for drawing lessons from nature, materials scientists have to abstract the basic principles and the major constraints at work in living organisms before designing their own behavior and strategy. The promises of self-assembly for nanotechnology have thus prompted a number of research programs in molecular biology and biophysics aimed at undestanding the process of self-assembly such as protein-folding or the use of templates generating geometrical constraints.

As a result it is clearly established that self-assembly requires at least two conditions: i) reversibility is crucial for allowing the readjustement of parts. Self-assembly relies on non-covalent bonds suh as hydrogen –bonding, electrostatic or ionic bonds and labile interactions. ii) the information must be contained in the reagents, encoded in the components rather than provided by an external program.

Ironically the study of the basic principles of self-assembly led to conclusions emphasizing the distance between organisms and machines. This is a major result of nanobiotechnology that goes usually unnoticed. In biomimetic strategies, the convergence between nano and bio does not rest on similarities. Rather it requires the clear recognition of the differences between biological and technological environments..A number of contrasts are listed in the tentative chart below which should be refined and probably extended.

Table 3 Contrasts between natural and artificial designs

Living Systems	Human technology
Ambiant Temperature +	High temperatures (difference needed)
Low energy (ATP)	High energy
Mobility of the components Brownian motion	No or few flucturations
Order out of noise	Noise as nuisance
Plasticity: conformation changes in response to environment	Rigid components
Adhesive Surfaces (van deer Waals)	Separated Surfaces
Variable number of components	Fixed number of components
Instructions for assembly inherent in the components	Instructions for assembly from outside
Local equilibrium between forces	
Correction through trials and errors	Central Control
Robustness through stochasticity	Robustness through redundancy

Emphasizing the contrasts between conventional engineering and biological processes was typically Richard Jones's enterprise in *Soft machines*.[19] In particular, Jones insists that biological machines work with Browian motion and that "a different feature of the physics

[18] Self-assembly is a typical example of biomimetics in the Aristotelian sense.When Aristotle defined *technê* as the *mimesis* of nature, he did not suggest that artifacts were copies of nature and rather that they resulted from an attempt at unveiling the sense (both meaning and direction or *telos*) of a production.

[19] Jones (2004)

that leads to problems for one type of design may be turned to advantage in a design that is properly optimised for this different world". [20] The properties characteristic of the nanoscale, which are problems for conventional machines, will have to be used as positive opportunities by nanoengineers. Jones thus contrasted two "design philosophies" to make nanoscale artefacts. Conventional design is based "on the principles that have served us so well on the macroscopic scale would rely on rigid materials, components that are fabricated to precise tolerances, and the mutually free motion of parts with respect to each other. As we attempt to make smaller and smaller mechanisms, the special physics of the nanoworld - the constant shaking of Brownian motion and the universal stickiness that arises from the strength of surface forces - will present larger an larger obstacles that we will have to design around". [21] Nanodesign should be based on the principles used by cell biology, labelled 'soft engineering'. It should not "treat the special features of the nanoworld as problems to be overcome, instead it exploits them and indeed relies on them to work at all".[22]

Given such differences, to what extent bio-inspiration may provide engineering principles? So striking is the contrast in Jones's book that his notion of "machine" sounds odd. It conveys near-fantastic and surrealist images *à la Dali*. Alfred Nordmann recently argued that Jones does not really provide an example of bio-inspired machine. He is not really concerned with technology. Nature provides an ideal that will never produce real machines but "phantom machines" - teleological ideals rather than technological solutions. However, soft engineering provides clues for highly "concrete technology" in the technical meaning of this term. The term "concretization" is used by Georges Simondon, a French philosopher of technology.[23] Concretization precisely consists in turning obstacles into conditions. A concrete machine works precisely because of (and not despite) its association with a specific environment. The environment where the machine will operate is not an external feature or a simple parameter that engineers have to take into account in the design process. The milieu is not something to which the machine will have to be adapted; it is an intrinsic aspect of the design of the machine. This is the major lesson provided by biological processes of self-assembly.[24]

Jean Marie Lehn who developed bio-inspired self-assembly strategies in supramolecular chemistry moved on to a program of "dynamic combinatorial chemistry", which emphasizes another aspect of biomimetics. Lehn's "Aufbau strategy" relies on the information stored at the molecular level. But information is processed through interactions between molecules. Self-assembly requires an "internal communication" between the components[25] , so to speak a society of molecules. "A glass of water is not like a water molecule", Lehn often says to stress that isolated molecules do not behave like interacting molecules. After inducing molecular recognition between artificial receptors and their substrates, the next step is to build up

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[20] Jones, R. (2004), p. 86
[21] Jones, R. (2004), p. 127
[22] Jones, R. (2004), p. 127
[23] Simondon (1989)
[24] Whether biological systems designed by Darwinian evolution are optimzed or not is the matter of ongoing debates. S.J. Gould, R.C. Lewontin, (1979) For Jones biological systems are optimized and provide a norm rather than inspiration for nanotechnology. "The insights of molecular cell biology show us more and more clearly how optimised nature's machines are for operation at the nanoscale. …] Nature has evolved to get nanotechnology right.(p.7) By contrast, Whitesides points out a major limit of bio-inspiration for self-assembly: biosystems do not make use of magnetic interactions which could prove very promising in technological systems because they are rather insensitive to environment. But here is precisely the key feature of self-assembly in biological systems. It is a process involving environment-sensitive properties, and responding to environmental changes.

[25] Lehn (2006)

systems through the controlled self-assembly of supramolecular architectures. And the third step is to induce adaptation and evolution. Lehn's dynamic combinatorial chemistry can be described as a program mimicking Darwinian evolution. The components mixed in a solution explore the possibilities of binding and this dynamics ends up with the correct double helix. Unlike the lock and key static model of recognition, which presupposes that the correct target has been identified, in this process the lock and the key select each other, through a random process of interactions. The basic concepts are "from static to dynamics, from real to virtual, and from prefabricated to adaptive". [26] The solution in the vessel potentially contains all possible combinations between the components. Or to go back to the car metaphor, the box contains not just the parts of one car, but the parts of all possible cars (from 2 CV to Formule 1) and the output depends on mutual adaptation. This blind process is not unlike the process of creation of order out of chaos in ancient Greek atomisitic cosmogonies. Lehn insists on the analogy with artistic creations in poetry and music such as Pierre Boulez's combinatorial composition. [27]

Strategy N°3: Integration

Integrative technology is a program carried by Carlo Montemagno, an engineer and professor of Biomedical Engineering at UCLA. It combines both previous strategies since the purpose is to hybridize living and non living systems, and to make artificial devices mimicking membranes or muscles. Most research projects are oriented towards biomedical applications. However the ambition is to create systems that offer emergent capabilities through extensive use of nature's models of molecular interactions and supra molecular assemblies..
« Integrative technology, the fusion of Nanotechnology Biotechnology and Information technology, provides the ability to build artificial organelles, functional units that manifest emergent properties that result from the stochastic non-linear interactions between the components of the system." [28]
Membranes are key actors in this program, because of their multiple functions: they determine the spatial organization, supply electricity, sense and relay information, detect specific molecules. On this basis it is conceivable to engineer an artificial membrane that processes information in a biological sense, and responds to its environment. For instance, the project aimed at producing excitable vesicles is explicitly conceived as an illustration of the emergence of higher-order properties.[29] By incorporating ion channels into a biomimetic membrane the purpose it to make a responsive system that will generate ionic currents when stimulated. Then by treating each vesicle as a neuronal mode the next purpose is to engineer computational units. Systems of excitable vesicles should be capable of performing various functions of the brain. It would execute rapid and precise pattern recognition from incomplete data sets, and process information from different sources.

The integrative program is grounded on a specific view of living systems. Here again nature is viewed as an "insuperable engineer" who builds-up machines. But the machine metaphor is much more precise than in the hybrid techniques previously described. The machine is a computer, an information processor. As much as biochemistry, artificial intelligence and neuronal studies of the brain provide the grounds for such projects. This view shared by the leaders of the NBIC program seems to be widespread in the nanotechnology community. For

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[26] Lehn 1999.
[27] Lehn (2004)
[28] Montemagno (2004) p. 39
[29] Montemagno (2004)

instance one can read in the French senate report on nanotechnology: « DNA computer tries to take inspiration from a rather efficient model of computer existing in nature, i.e. living organisms ». [30]

This overarching model casts doubts on the ambition to build up complex devices. Computers are not really complex machines so that the non-linear effects should come out from the hybridization with biocomponents. The ultimate aim of Montemagno's integrative strategy is to mimic the brain activity with artificial vesicles, with units performing a specific task. In more philosophical terms, the ambition is to design a complex machine, modeled after a Cartesian machine. Ironically the so-called "integrative technology" is not deeply concerned with how to integrate artifacts within biological environments. How to avoid adverse effects due to immune responses is not an issue. And the least concern is how to get the artifact work together with the biological environment in order to make a "concrete machine". Integration is not an issue because the underlying assumption is that molecules, cells and neurons are of the same nature, they are all computer-like. A true integrative approach to self-assembly requires an emphasis on the contrasts rather than on the similarities between human technology and living systems. And it could be a more promising route to build up concrete machines.

To sum up this section, the three types of self-assembly strategies here outlined are based on quite different views of nature. In Strategy N°1, and Strategy N°3, nature is viewed as a collection of independent devices and machines that can be put at work in artificial machines. In Strategy N°2, nature is viewed as a system relying on "a special physics". Hybridization is a strategy inviting a process of fabrication. It requires both a designer - a clockmaker who designs an overall project or a player who has the whole picture of the jigsaw puzzle – and a strict control of the process, In strategy N°3 combining hybridization and mimicry there is also a designer although the project is to build a system that manifests functionality not constitutive of its components, with emerging properties. By contrast, strategy N°2 of biomimetic self-assembly is a blind process of creation through combinations and selection without external designer. Even when biomimetic chemists are doing "directed self-assembly" or "self-organization by design" they do not claim to secure a strict control of all steps and they have to be prepared for unexpected results.

Such opposite worldviews may well result in alternative technological styles. For chemists such as Whitesides and Lehn, self-assembly is not a key for nanotechnology. Whitesides insists that self-assembly is not confined to the molecular level and noted that biological structures are relatively large compared to the devices designed in nanoelectronics or nano-optics.[31]. He even stated that self-assembly is more suitable and more promising at the mesoscale. [32]

Lehn is even more radical in divorcing self-assembly and nanotechnlogy. For him self-assembly and dynamic combinatorial chemistry offer an alternative to nanotechnology attempts at working with individual and isolated molecules..[33]

Table 4: Strategies of self-assembly

HYBRIDIZATION	MIMICRY	INTEGRATION

[30] Saunier C (2005) vol. 1, p. 70
[31] Whitesides, 2003, p. 1161.
[32] Whitesides, Boncheva, 2004
[33] Lehn 2004 p. 2462.

Nature provides solutions to engineering problems	Nature gives lessons of engineering	Nature provides a model of emergence
Nature viewed as a collection of devices	Nature viewed as a system	Nature viewed as a computer
Emphasis on similarities between nature and artifacts	Emphasis on differences between nature and artifacts	Emphasis on continuity
Control	Creativity	Emergence

II. Conceptual distinctions and their implications

The two terms self-organization and self-assembly are often used interchangeably and sometimes in association. The boundary between the two notions seems rather elusive and elastic in current literature. The purpose of this section is to emphasize the significance of the distinction (or non-distinction) between the two notions.

The two notions originated in very different contexts. Whereas the term self-assembly emerged in the 1980s in organic chemistry and Materials Science & Engineering, the term self-organization, introduced in the late eighteenth-century by Immanuel Kant to mark the distinctive features of organisms, became extremely fashionable in the 1970s. According to Isabelle Stengers's genealogy, self-organization is a notion issued from two different traditions in the 1960s: from cybernetics, in particular John Foester's Biological Computer Laboratory created in 1958, and from physical chemistry, in particular Ilia Prigogine's work.[34] While self-organization was not really central in these two research traditions, it became the hard core of Henri Atlan's research program in 1972, with the publication of *L'organisation biologique et la théorie de l'information*. Thereafter the term self-organization permeated a number of registers such as fine arts, economics and politics.

Self-organization is in itself a polymorphous notion. For Ashby, it meant evolution of a system toward equilibrium state, and applied to closed systems. For Prigogine it is evolution toward steady-states, which means that self-organized systems are open systems. For John Von Foerster, self-organization means order from noise with decrease of relative entropy, and increase of redundancy within the system. Although Atlan also assumed the view of self-organization as order from noise, he insisted that it was complexity from noise. In his view based on Shannon's information theory, self-organization is a process requiring a hierarchical multilevel system and initial redundancy, so that it leads to a decrease of redundancy.

How are we to characterize the relations between this notion with a rich and multi-facetted past and the more recent concept of self-assembly? To what extent do they refer to the same processes? Do they belong to the same order?

Looking at the recent literature, there are several attempts at distinctions but no consensus about criteria of distinction.

Thermodynamic perspective

The most common distinction between self-assembly and self-organization has to do with thermodynamics. In thermodynamic terms, self-assembly is due to the minimization of free energy in a closed system. It leads to equilibrium state. For instance, phospholipids with hydrophobic and hydrophilic ends placed in aqueous solution spontaneously form a stable structure. Self-organization only occurs far from equilibrium, in open systems, as it requires external energy source. It is a production of order out of irreversible process with energy dissipation. It is a local phenomenon illustrating the significance of singularities, out of the

[34] Stengers (1985)

scope of statistical mechanics.

This clear-cut distinction between self-assembly and self-organization is strongly recommended by Richard Jones. "People use different definitions, but it seems to me that it makes lots of sense to reserve the term *self-assembly* for equilibrium situations. […] We can then reserve self-organisation as a term for those types of pattern forming system, which are driven by a constant input of energy. A simple prototype from physics are the well-defined convection cells you get if you heat a fluid from below, while in chemistry there are the beautiful patterns you get from systems that combine some rather special non-linear chemical kinetics with slow diffusion - the Belousov-Zhabotinsky reaction being the most famous example. "[35]

Chemical perspectives

By contrast, George Whitesides defines two types of self-assembly: the static one - resulting in equilibrium state- and the dynamical one, with energy dissipation.[36] Dissipative structures are thus considered as examples of self-assembly. To be sure Whitesides deplores the current abuse of the term self-assembly and tries to provide a more focused definition: "'Self-assembly' is not a formalized subject, and definitions of the term "self-assembly"seem to be limitlessly elastic. As a result, the term has been overused to the point of cliche´. Processes ranging from the non-covalent association of organic molecules in solution to the growth of semiconductor quantum dots on solid substrates have been called self-assembly. Here, we limit the term to processes that involve pre-existing components (separate or distinct parts of a disordered structure) are reversible, and can be controlled by proper design of the components. "Self-assembly" is thus not synonymous with 'formation.'[37] Despite his efforts to limit the notion Whitesides's definition embraces a wide variety of processes ranging from crystallization on surfaces, templated synthesis to cell's functions and schools of fish.

Table 5 . Examples of self-assembly (S, static, D, dynamic, T, templated, B, biological). from Whitesides, Grzybovski, 2002.

System	Type	Applications/importance
Atomic, ionic, and molecular crystals	S	Materials, optoelectronics
Phase-separated and ionic layered polymers	S	
Self-assembled monolayers (SAMs)	S, T	Microfabrication, sensors, nanoelectronics
Lipid bilayers and black lipid films	S	Biomembranes, emulsions
Liquid crystals	S	Displays
Colloidal crystals	S	Band gap materials, molecular sieves
Bubble rafts	S	Models of crack propagation
Macro- and mesoscopic structures (MESA)	S or D, T	Electronic circuits
Fluidic self-assembly	S, T	Microfabrication
"Light matter"	D, T	
Oscillating and reaction-diffusion reactions	D	Biological oscillations
Bacterial colonies	D, B	
Swarms (ants) and schools (fish)	D, B	New models for computation/optimization
Weather patterns	D	
Solar systems	D	
Galaxies	D	

Thus Whitesides extends the realm of self-assembly to all length-scales from atoms to

[35] Softmachine blog, Nov 15 2005
[36] Whitesides, Grzybovski, 2002.
[37] Whitesides, Grzybovski, 2002. p.2418.

galaxies via biology.[38] Far from confining self-assembly to the nanoscale, Whitesides and his collaborators argue that self-assembly works at all scales and that its future lies primarily at the mesocale.[39]

On the other hand, Lehn uses both terms more or less interchangeably to characterize the synthesis of supramolecular architectures. He just assumes that self-organization is self-assembly with the production of a precise structure – such as double-helix metal complexes and pentagonal or hexagonal grids, depending on the nature of the metallic ion used. He insists on interactions between molecules and their collective behavior. Considering that isolated molecules do not behave like interacting molecules, that a glass of water is different from of water molecule, Lehn assumes that something emerges from their "being together". Togetherness was precisely one major feature of Prigogine's notion of self-organization according to Isabelle Stengers. It implies not only "being together" but "acting together", a collective behavior which results from coupling processes rather than just expressing information contained in the components. Thus for Lehn, controlling the basic forces of self-organization is the ultimate aim of chemistry.

❖ *Biological Perspectives*

The contrast is striking between chemists who assume continuity between self-assembly and self-organization and biologists who tend to draw clear boundaries. Whereas Whitesides defines two varieties of self-assembly, two biologists Kirschner and Gerhart insist to delineate two kinds of self-organization.

Kirschner and Gerhart devoted an important paper to conceptual issues entiled "Molecular vitalism". [40] They agree with Whitesides on the analogy between assembly resulting in equilibrium and assembly with energy dissipation. They argue that for a single cell, there is no difference of nature between self-assembly and self-organization. At the level of one single cell, self-organization is just an extension of self-assembly employing chemical strategies in order to break symmetry. The formation of ordered aggregates by the self-assembly of identical components generates an asymmetry and leads to polarization. So polarization and regulation – two characteristics of self-organization in single cells – may be viewed as simple extensions of self-assembly. By contrast, when self-organization occurs at the system level (for instance in embryos) it is a quite different phenomenon. First, it involves exploration of an assembly landscape and selection of a functional steady-state. Whereas self-assembly works best in a set of predetermined conditions, in self-organization the final state may change in response to changing conditions. This is crucial for resilience and adaptation. Second, self-organization implies a diversity of states. This requirement is also a major characteristic in Atlan's view of self-organization. It is important because self-organization demands no accuracy on cell number and position because the diversity of states is in itself an important parameter, offering possibilities for selecting between states.

As a philosopher of biology reflecting on the role of self-organization in the origin of life, Evelyn Fox Keller located the boundary elsewhere in order to emphasize the novelty of selection.[41] She rejects the common distinction between self-assembly near thermodynamic

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[38] see Table 1 in Whitesides, Grzybovski, 2002
[39] Whietsides, Boncheva, 2002.
[40] Kirschner and Gerhart (2000)
[41] Fox-Keller (2006)

equilibrium and self-organization in energy-dissipating systems. Like Whitesides she assumes that self-assembly – “another word for composition”- is a form of self-organization, a dynamic process responsible for the emergence of metabolism, an entirely chemical process. While she blurs any real boundary between self-assembly and self-organization, Fox-Keller argues that two differences need to be marked: “between the iterative processes of self-organization that occur over time, and the one-shot, order-for-free, kind of self-organization associated with the non-linear dynamical systems that mathematicians usually study; and second, between the heterogeneity of complex systems and the uniformity of simple gases, lattices, or fluids, or finally, between multi-level structures and horizontal structures”. She assumes that the iterative process of self-assembly may be responsible for most evolutionary processes prior to Darwinian selection. The process of selection of the fittest emerged out of more basic processes of selection of stable structures. But for selecting the fittest among a crowd of possible stable units, an algorithm is needed that self-organization does not provide. And here is the genetic threshold.

Indeed one may ask: Does it really matter whether dissipative structures are viewed as a variety of self-assembly or as a variety of self-organization? Who cares for the multiple meanings and different extensions of the notions of self-organization and self-assembly? In most natural sciences, definitions are a matter of convention, and sometimes a matter of convenience. Loose boundaries occasionally proved fruitful to the advancement of science. Moreover they testify to the fact that this concept is very successful. From the point of view of the dynamic of knowledge, Sabine Maasen argues that “the price of a term being successful is its increasing vagueness – and the perceived need for each individual field of research to define (and hence limit) its use.”[42]

❖ *Science War?*

It is precisely the dynamics of knowledge, which is at stake in this conceptual distinction. It has to do with the demarcation between the respective territories of chemistry and biology. Jones’s criteria of demarcation based on equilibrium and far from equilibrium draws a clear-cut boundary assigning self-assembly to physicists and chemists while self-organization remains the major feature of life. “Self-assembly is not in itself biology, it is used by biology. A system organized by equilibrium self-assembly is moving toward equilibrium and things at equilibrium are dead.” [43] Jones claims that although information stored in the sequence of amino-acids accounts for protein folding, life is more than just information; it is also metabolisms. Nevertheless the physicist’s approach is relevant to increase our understanding of biological systems in so far as life is not an isolated system and complies with thermodynamics second law.
In characterizing self-organization in living systems, Jones describes something very similar to Von Foerster’s and Atlan’s notions of self-organization. Atlan already insisted on the originality of self-organization, by stressing the contrasts between biology and human technologies. Noise, a major obstacle for engineering projects is the condition for generating order in “natural machines”. Living organisms turn our major obstacles into operating conditions. « Noise, for the former [communication engineers] is a bitter pill, for the latter

[42] Maasen, 2006
[43] Jones softmachines blog March,14, 06 *How much should we worry about bioNT ?*

[biology] it is the spice of life. Redundancy for communication engineers is a burden. It is a bonus for biologists ».[44] Moreover Atlan characterizes self-organization by its creative power. On the basis of a study of immune systems, he argues that self-organization is more than a creation of information out of noise it also creates "meaning".[45] The discrimination between self- and not-self is not just a deterministic reflex programmed in the genes. It is described as the result of "a dynamic process of continuing challenges and responses". [46] Thus self organization becomes a process of individuation, which is radically different from self-assembly. Self-assembly may result in the production of aggregates but it will never generate an individual unit, since for Atlan the individual is not a product of some obscure mechanism, it is the process itself of interactions with a unique environment.

Such distinctions are strategic for delineating territories between rival paradigms. Kirschner's and Gerhart's distinction between two varieties of self-organization help them emphasize the limitations of the chemical approach to living systems. They deplore the domination of genetics and molecular biology over biology and see the future in a revival of physiology. « In a light-hearted millenial vein we might call research into this kind of integrated cell and organismal physiology « molecular vitalism.» [47] Consequently Kirshner and Gerhart claim that it is time to move beyond the genomic analysis of proteins and RNA components of the cell in order to understand the robustness of biosystems.

By contrast, Whitesides's strategy of expanding the domain of self-assembly is in keeping with his belief that chemistry is everywhere and must go everywhere.[48] Chemistry so far confined to the interactions between atoms and molecules using strong covalent bonds is expanding its territory, by using the whole spectrum of weak forces and operating at various scales. Chemical language can decipher the most complex phenomena: "The nature of the cells is an entirely molecular problem. It has nothing to do with biology".[49] And since neurons also use chemical mediators, chemists should also contribute to merge silicon electronics with the brain.

Similarly Lehn's program of Constitutional Dynamical Chemistry revives the greatest ambitions for chemistry. His program evolving from supramolecular chemistry to dynamic combinatorial chemistry looks like a modern replica of Berthelot's grandiose program of synthetic chemistry, which would gradually lead him, step by step, to more and more complex compounds and ultimately to the frontiers of life.[50] Lehn portrays chemistry as the "science of informed matter", a core science mediating inanimate matter (materials process) and animate matter (living organisms and their complex behaviours).[51]

Self-assembly has revived the chemists' ambition to access the "essence of life". As Philip Ball rightly points out, chemists are now addressing the "big questions" about the Big Bang and the origin of life. Far from confining their work to the production of utilities, chemists want to address questions about the origin of life and of consciousness: "For me, Lehn says, chemistry has a most important contribution to make to the biggest question of all: how does

[44] Atlan H, Cohen I.R., 2006, p. 125.
[45] Atlan, Cohen, 2006.
[46] Atlan, Cohen, 2006, p. 137

[47] Kirschner, et al. 2000, p. 79.
[48] Whitesides, 2004.
[49] Whitesides quoted by Philip Ball (2006) p. 501.
[50] See Bensaude-Vincent & Stengers (1996) p. 152-154
[51] See Lehn 2002 Table 3 on p. 2402.

self-organization arise and how does it lead to the Universe to generate an entity that is able to reflect on its own origin?"[52]

To an outside observer, this expansionist attitude strikes as being at odd with the current consensus about the merits of cross-boundary research and interdisciplinary programs. How is possible to hear such passionate advocates of a discipline when the leaders of the program *Converging Technologies* announce that the age of scientific specialties is over: "The sciences have reached a watershed at which they must unify if they are to continue to advance rapidly. Convergence of the sciences can initiate a new renaissance, embodying a holistic view of technology based on transformative tools, the mathematics of complex systems, and unified cause-and-effect understanding of the physical world from the nanoscale to the planetary scale."[53] Although interdisciplinary teams and cross-boundary research programs are flourishing and have demonstrated their efficiency on some occasions, it seems that the grand unifying understanding of the world is neither for today, nor for tomorrow… unless unifying means reducing everything to atoms and molecules. There are still a few notions that can fuel science wars.

As Stengers argues, the issue of emerging properties, of the parts/whole relationship has always been a niche of conflicts.[54] From Aristotle to Dawkins it has been raised in polemical contexts and generated battles between reductionists and emergentists. It is precisely because self-organization and self-assembly are related with this issue that they continuously reconfigure the map of knowledge. In the 1960s, self-organization supported projects of reorganization of disciplines. Despite different approaches, the cybernetics and the physical-chemistry traditions shared the same ambition to interfere with life sciences, to show the relevance of their discipline to understanding the singularity of living systems. Self-organization in cybernetics was an attempt to understand living systems through a new generation of machines (after the clock and the steam engine) whereas for Prigogine the challenge was to reconcile the biological order with the second principle of thermodynamics by introducing the time arrow in physics. In fact, according to Stengers, Prigogine took his notion of self-organization from embryologists who used this term in response to the failure of attempts at identifying a specific chemical substance that would induce the process of organization in early embryos.[55]

So the specificity of biological systems was already a matter of controversy in the dual origin of the notion of self-organization, since cybernetics refused any a priori distinction between organic and inorganic system, whereas embryologists reserved the term self-organization for biological systems.

A dividing line

Thirty years later, the notion of self-assembly seems to re-open the debate along more or less similar lines. The fireline between the emergentist and reductionist camps no longer follows disciplinary boundaries. The map of the battlefield is more complex. Whitesides and Lehn claim that their views of chemistry are not reductionist. Lehn insists that it is chemistry, which is becoming complex, adaptive and evolutive. Whitesides claims that chemistry so far was « blindly reductionist » and that chemists will have to move « beyond molecules to learn the entire problem ».[56] Just as Prigogine's ambition was not to reduce biological systems to

[52] Lehn quoted by Ball (2006) p. 501.
[53] Roco, Bainbridge 2002, p. xii
[54] Stengers (1997)
[55] Stengers (1985) p. 36
[56] Whitesides, 2004.

physics or chemistry, both of them assume that chemistry has the power to explain living systems because chemistry in turn is deeply transformed by its application to complex phenomena. Just as Prigogine imported in physics the problem of collective behaviour or « how to act together » that had been raised by embryologists in their use of the term self-organization,[57] Lehn is importing the same problem at the molecular level. If you look carefully at the collective behaviour of molecules, there is plenty of room for complexity at the bottom! It is no longer the landmark of living systems.
On the biologists' side, Atlan, Kirschner, Gerhardt and others are also fighting against reductionist temptations in molecular and cell biology. Today the fireline could be located within the biology community – between system or network biology and synthetic or chemical biology.[58]
Thus the fireline between emergentists and reductionists has significantly shifted. It is no longer a matter of disciplinary affiliation because the distinction between living and non-living does not really make sense at the nanoscale. In fact, in various scientific communities - physics, chemistry, biology, artificial life, etc - a number of individual scientists are using self-assembly or self-organization as watchwords against reductionist trends. In this perspective, the emphasis is less on the prefix "self", than on the notion of organization. The difference between "assembly" and "organization" becomes a difference in degree of complexity rather than a difference of nature. Although the notion of assembly connotes technology (assembly line) while the notion of organization connotes biology (organism), the contrast between assembly and organization is not referred to the divide between art and nature. In keeping with the etymology of the Greak term *organon* (tool or instrument), the phrase self-organization suggests an analogy between the making of living organisms and the making of artefacts. Both terms belong to traditions, which assume the validity of the machine metaphor for organisms. From the outset, self-organization was characterized in engineering terms by cybernetics,[59] and we have seen that the phrase self-assembly was clearly introduced as a design principle, a new style of biomimetic engineering.
However the prefix "self" needs clarification as it could serve to delineating diverging views of machines. In the first cybernetic tradition, the notion of "self" referred to the function relating internal states and inputs. By contrast, in von Foerster's Biological Computer Laboratory, the notion of "self" marked the distance from first generation machines as it meant that the system was organized without external organizer, the program being within the structure.[60] There is a similar distance between the strategies of self-assembly described in the first section. In hybridization strategies as well as in the so-called integrative approach, the "self" refers to a functional device, which is part of a machine. The result is a logical machine embodied in a physical structure. By contrast in biomimetic strategies, "self" refers to population of interconnected molecules exploring the various possibilities of collective behaviour.

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[57] « Prigogine n'apporte pas une « loi physique » nouvelle, un nouveau type de molécules ou d'interactions, ce qui aurait eu pour conséquence, certes d'enrichir la physique, mais aussi de réduire la biologie à la physique, comme la chimie l'a apparemment été avec l'interprétation quantique des liaisons chimiques. Il s'agit d'une extension de la notion « d'être ensemble », qui légitime du point de vue de la physique, les questions posées par les biologistes, mais sans les résoudre pour autant ».
Stengers (1985) p. 82
[58] On Network Biology see Barabásí 2003, Barabásí & Bonabeau 2004, Barabásí &Oltvai, 2005, on Synthetic Biology see *Nature*, 438, 24 November 2005, 417-18 and *Nature Chemical Biology* , 2, N°6, June 2006
[59] In *Entre le cristal et la fumée*, Henri Atlan described the cybernetic neo-mechanicist approach to organisms through a parallel between natural and artificial machines. Pointing out the differences was his purpose but Atlan did not question the validity of the analogy and the machine metaphor. Atlan, 1979.
[60] See Dupuy (2000)

III) - Ethical implications of the « without human intervention »

To what extent self-assembled and self-organized artifacts challenge the conventional view of artifacts as man-made products? How are we to look at devices and machines made by materials themselves "without human intervention"? Are they the works of nature rather than the products of human design? To what extent changing the process of making will affect the designer's responsibility?

Indeed all artifacts are both artificial and natural as Descartes noticed in the *Principles of Philosophy* in so far as they use nature as a stock of raw materials or energy, and obey nature's laws. However, Cartesian classical machines differ from self-assembled systems. Although it is possible and useful to describe self-assembled proteins in terms of input and output, they do not follow the same design principles.

Self-asssembly is not a "human fabrication " in the sense that the assembly process is not operated by human hands or tools. In this respect even a robot performing human tasks is different because the robot is just a more sophisticated mediation. In self-assembly there is no need of mediation since the constituent parts themselves determine the assembly process. Conventional top-down technologies follow norms or standards that do not exist in nature. The standards have been imposed by generations of artisans and engineers. By contrast in the bottom-up way where the maker adjusts natural entities so that they can operate by themselves, no human norms or standards are imposed on the process. Unlike the designer who imposes rules on nature so that nature eventually would become his possession (cf Descartes' s 'maitre et possesseur') the designer arranging self-assembly allows nature's operations in the course of artificial manipulations instead of imposing a norm. In other terms the normative power shifts from man to nature. In this respect self-assembly is more like a generative process than a fabrication process.

Generation could be a more appropriate term than *fabrication* and *creation* as well to refer to such processes because it avoids the God-like connotations of the term "creation". Self-assembly is not « an engine of creation»; it does not imply self-replication. Self-assembly and self-organization are spectacular and impressive phenomena but they have nothing to do with the self-replicating robots that triggered science-fiction visions. Self-assembly is not subjected to the playing God accusation and would rather invite the literary genre known as "the marvels of nature", which flourished in nineteenth century popular science and so well served natural theology. The term *generation* is also relevant as long as the metaphor of birth-giving reminds us that « without human intervention » does not mean « without human initiative » or « without human project ». Whatever the strategy used, self-assembly is nothing like leaving natural process alone. Self-assembly is a natural process taking advantage of nature's laws (Carnot's principle for instance), for performing a useful task. But it is by no means a blind or unintentional process.

However the control of spontaneous processes is not like the control of Cartesian machines. The clockmaker designs each constituent part for performing a specific task, necessary for the operation of the whole mechanism. Thus the machine is virtually under strict control, transparent to its designer, who knows and manipulates the variables that continuously modify the operations. This is the kind of control that the slogan of the National NanoInitiative "shaping the word atom by atom" sought to convey. Nanomachines are presented as instruments operating under strict control, even though they rely on mechanisms with too many variables.

This image of full control is totally misleading for characterizing the integrative approach (strategy N°3), since it explicitly aims at losing control, at generating complex systems. As complex systems are known for their robustness and vulnerability, the designer are responible for what they become. As Jean Pierre Dupuy argues, they are managing objective uncertainty and irremediable unpredictability.[61] The only prediction is that the third generation nanotechnology products will lead to systems of systems, which become more and more autonomous. And the International Risk Government White Paper gives a list of potential high-risk products.[62]. However, it is not just a question of avoiding risks, a precautionary attitude is needed. Since Dupuy has often insisted on this important aspect, I will not discuss it further and rather point the ethical issues raised by Strategies N°1 (hybridization) and N°2 (biomimetics).

As for hybdization strategies, transposing the model of Cartesian machines to the design of hybrid devices using the assembly power of biological materials is also problematic. To be sure from a moral standpoint there is no problem in using engineered DNA sequences as man-made tools to build up machines, as long as these sequences are entirely artificial. It is not like using domestic animals to carry canon balls or coal wagons in the mines. However the designer is responsible for the behavior of the DNA sequences and their interactions with the environment. As long as living systems are viewed as a collection of nanomachines, it is urgent to think about the uncontrollable interactions between natural and artificial nanomachines. How those nanomachines fit together and how they operate into a complex system is still unclear. Today nanobiotechnology is not precisely well equipped for understanding the complex relations between the technosphere and the biosphere as long as the attention has been mainly driven to building up tiny devices. Despite its ambition to revisit the foundations of quantum mechanics nanoscience tends to dissolve the unity of nature constructed by classical mechanism and twentieth century physics into a multitude of tiny machines. Nanoscientists hold the local but they loose the global view. A jungle of nanomachines is not a cosmos. It is thus the collective responsibility of decision makers in science policy to think about long-term consequences of this research priority.

What kind of control of the spontaneous process of self-assembly and self-organization is involved in biomimetic strategies? Biomimetic chemists are using interactions between molecules. As we have seen the intervening linkages are statistical rather than mechanical. There is no simple calculus for predicting a continuous variation of output. The label "self-organization by design" [63] used by Lehn to define his program does not mean that the designer gains full control over his or her creation. Rather it means inducing a process that delegates the task of building up to a "society" of interacting molecules. The situation is no radically different from that created by organic chemical synthesis. Synthetic chemists cannot physically see nor handle the parts to be assembled. They delegate the operations they want to perform to molecules, radicals, ions…. They rely on crowds of molecules, which do not behave like hammer in the hands of workers. As Primo Levi, the chemist-turned-writer put it,

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[61] Dupuy (2004)

[62] International Risk Governance Council White Paper on Nanotechnology Risk Governance » June 2006 , www.irgc.org, p. 23 The list includes : emerging behaviour robotics, evolutionary artificial organs, modified viruses and bacteria, and brain modification. Several potential higher-risk areas are: nanorobotics; regenerative medicine; brain-machine interface; nano-engineering in agriculture; nanosystems used for manufacturing and product processing; and other converging technologies and applications

[63] Lehn 2004

synthetic chemists are like blind elephants operating in a jewelry workshop.[64] The chemist "delegates" tasks to molecules and put them at work for her. The result of their design is not entirely the product of their hands and brain. It is mainly the offspring of a spontaneous process. In this respect, chemist and material scientists who design self-assembled structures do not have the same responsibility as the clockmaker. Their position is more like that of parents (generators) responsible for their offsprings. Like parents, scientists and engineers are responsible for their artifacts and for what they become in a fluctuant and unpredictable environment.[65]

Thus the term *generator* seems more adequate than *homo faber* to characterize the kind of responsibility involved in the design of self-assembled structures. Nevertheless because of its biological root the term *generation* is misleading since it tends to "naturalize" the design of artifacts and overlooks their social and cultural dimensions. Therefore I suggest the term *pilot* of self-assembly and self-organization as a more adequate alternative to the paradigm of *homo faber*. Pilots rely both on natural elements and instruments to guide their sea boat. They know that all journeys are risky, that their jobs involve a good deal of uncertainties. They negotiate with nature rather than resting on nature for the success of their enterprise.

References to nature are never neutral. Although nanotechnology continuously blurs the divide between nature and artifact, nature is often invoked in the literature about nanotechnology. The most obvious intention of repeated references to nature is to assuage the public's fears about nanotechnology. For instance A European Commission brochure issued in 2004, claimed that « nanotechnologists are fond of nature" and that " nanotechnology is based on pure nature". [66] The underlying deduction is that if nature itself uses nanotechnology, then it is not dangerous. If "life is nano" then nano should be accepted without fear and without discussion. Natural is used for good and healthy. Nature here acts as a norm, delivering a moral permission to pursue the exploration and exploitation of the nanoworld.
More importantly a number of nanoscientists refer to nature in order to get the licence to achieve their project. The underlying deduction is: if nature does it, then we are able to do it. For instance, Drexler argued that if biological systems are able to self-assemble parts with ribosomes then human technologies can do it. Despite attacks from all sides against Drexler's assemblers, the reference to nature's nanotechnology is still in use, even by scientists who are well aware of the differences between "soft machines" and engineering design. In this case the reference to nature provides an epistemic value to laboratory creatures. The existence of similar designs in nature transforms laboratory curiosities into plausible machines. For instance the first rotaxanes and catenanes designed by Jean-Pierre Sauvage were just strange creatures of skilful synthetic chemists until it was found that similar machines are operating in nature, on the same principles. Then they became interesting creatures, with great potentials.

The importance of nature in a world where the art/nature divide is continuously challenged suggests that the dichotomy between *phusis/technê* (nature/artifact) that we inhereted from

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[64] Primo Levi,

[65] cf Whitesides A (2004) « We scientists do have something special to contribute to discussions about the outcome s of science » (p. 3641). However this sense of responsibility is immediately qualified by the addition "Human kind will do what it will do". So Whitesides had to conclude that the law of unintended consequences would apply.

[66] European Commission N*anotechnology, innovation for the world of tommorrow,* 2004, http://europa.eu.int/comm/research/rtdinfo/index-fr.html

Ancient Greek philosophers is extremely resilient. However we should never forget that it used to be complemented by another dichotomy between *phusis/nomos* (nature/convention) Precisely because there is no clear-cut boundary between nature and artifact, a threshold has to be set up by convention, by social decree or collective decision. It is our responsibility as citizens to make preconizations for placing the cursor between nature and artifact between life and inert matter at one point. This may be a religious matter or a subject for democratic debate in non-religious societies. A good balance between the three summits nature/art/culture/ is important to regulate the advancement (or maybe just the maintenance or survival) of our civilization.

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