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# Bio-inspired and Bio-inspiration: a Disruptive Innovation Opportunity or a Matter of "Semantic"?

## A Review of a "stronger than logic" Creative Path based on Curiosity and Confidence ($4C^2 2C^{©}$)

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**ABSTRACT:** "Innovation is not the idea, but what you do with it". Can ideation be engendered by artificial means? Can it come from bio-inspiration?

In this third review centered on innovation, open innovation, and now disruptive innovation, the authors have reviewed and re-contextualized various bio-inspired technologies ranking from pharmaceutical developments, medical treatments, software and hardware, energy, materials and natural polymers.

This after a refreshing introduction associated with 1- the skills of the "bio-inspired" business engineer, 2- the open innovation process path and discipline therewith and 3- the patent value of the pioneering, possibly disruptive inventions in the typical patent portfolio.

A knowledge flow pattern, from sharing, integration, search, generation, classification, dissemination, to application, is proposed to outline the necessary understanding of bio-inspiration to yield application of innovative value; still nurturing the proposed knowledge "life cycle".

The necessary creative confidence can be gained, reinforced by the bio-observation and inspiration; nonetheless a larger set of functions may need to take part to the innovation process with their own recognized and valued creative potential and phobia elimination.

When performed by enlarged teams comprising the engineer, scientist, IP strategist, business model expert, sales and marketing teams, accountant, executive and operating teams, the ATA©, adjacent technology analysis – covered in previous reviews - is one way to further challenge the imperfect patent tools when dealing with open disruptive innovation. Semantic is, in the present study, shown as an improvement, lacking motion and pictures.

**KEYWORDS:** Innovation, open innovation, disruptive innovation, collaborative, Collaboratory™, adjacent technology analysis, ATA©, IP strategy, semantic analysis, bio-inspired, bio-inspiration, pharmaceutical, medical, software, hardware, energy, materials, natural polymers, bio-mimicry, biotechnology, DNA, confidence, curiosity.

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*Some assessments are intended to educate and raise awareness of some of the complex issues that surround the intellectual property in the field of knowledge extraction from the about 80 million patent documents available, and to assist in the development of practical skills for dealing with inventions in the context of innovation. It does not seek to provide legal, managerial or technical advice on intellectual property related law as such. For any guidance, legal or any other, seek advice from the appropriate professionals; this study can by no mean substitute for expert legal, technical and managerial advice.*

*The opinions expressed by the writers in this article do not necessarily represent the viewpoints of the companies the author are employed by.*

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## 1 INTRODUCTION

### *Confidence and Curiosity, part of the broader Creativity*

As a continuation "chapter III" of an on-going innovation series appearing in IJIAS, Int. J. Innov. Appl. Stud., [1], [2] (Rebouillat & Lapray, 2014; Rebouillat, 2013), and prior to introducing this subject in the context of bio-inspired matters, it is probably desirable to remind the reader of some prerequisites; such as the skills generally anticipated to take an active part in the process of innovation, which is outlined within an R&D path from ideation to product launch. It is also equally important to position the intellectual property (IP), and more specifically the patent dynamics in these pre-introductory refreshing fundamentals.

After adding the Collaborative/Collaboratory® dimension to each and every 4C© skill descriptor introduced by Rebouillat back in 1998 [1], [2] (Rebouillat & Lapray, 2014; Rebouillat, 2013), two extra criteria revealed especially useful in the present study.

The business engineer, now unavoidably part of multiple networks, called most of the time the open innovation networks, such as many other partners in the process of innovation, will best perform his task if Curiosity and Confidence are promoted and stimulated by this process. There are many ways to avoid lack or loss of Curiosity and Confidence, which generally occurs out of personal experience, back sometime in the childhood and education journey, or which is inherently unavoidable due to an excessive standardization of the business/technology & science functions; splitting the creative from the non-creative people.

Kelleys (2013) [3] have authored one of the most astonishing essay on the matter of confidence in the creative course, involving a very large and diverse population and functions therewith. No doubt that although well-known hindrance circumstances, such as phobias, tend to annihilate creativity, the authors found ways to successfully develop and put in place methods to change the creative records of small to large organisations once the need is well recognized; sometime at the upper CEO&CTO levels to start with.

The word Curiosity tends to be subject to interpretation, pending on the context and multilingual semantic; in the present study its original meaning from the classic Latin language, *curiositas,* is favoured since it is associated with the care, i.e. special attention, and search, i.e. discovery, dual roots.

Mankind tends to "trust" nature and bio-events and therefore to gain confidence from the observation of nature and bio-systems; as long as sufficient curiosity is placed into the comprehension of these in order to limit usual phobias or to avoid leaning towards inhibiting ineluctability.

Bio-inspiration fits well with the addition of the 2C, coming from Curiosity and Confidence, to the $4C^2©$ equation, becoming $4C^2 2C©$, as depicted on figure 1.

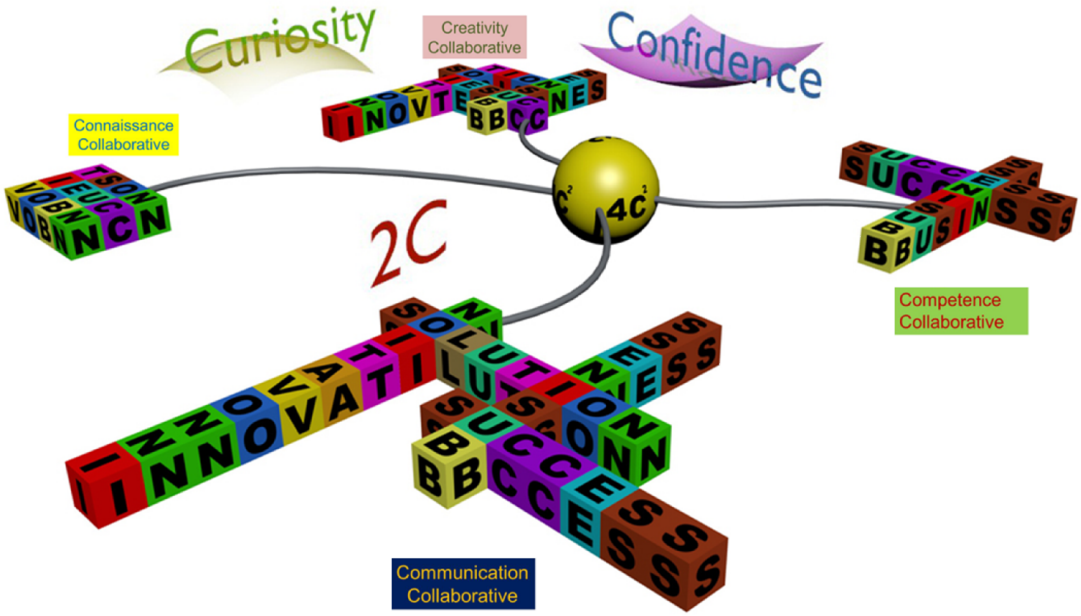


***Figure 1. Curiosity and Confidence now part of the 4C²© equation becoming 4C²2C©***

***"Management Processes" are part of a broader Creativity too***

There are several processes which may be used to safeguard creative developments and to help establish a multigenerational product roadmap with secured IP and business models therewith.

The House-of-Quality, the Quality Function deployment (QFD), the Voice-of-Customer (VOC), the Theory-of-Constraints (TOC), the integrated Theory of Inventive Problem Solving (TRIZ), Six Sigma, etc. have paved the way to promote best practices, to boost and to secure the innovation processes and routes to market of multigenerational products and processes [1], [2] (Rebouillat & Lapray, 2014; Rebouillat, 2013).

Most of these approaches, individually or integrated in innovation management processes, have now got Wall Street's attention and became prerequisites to a good design of a portfolio of products. Although not so long ago Business Models were missing or developed as an after the fact "justification" or became the "most natural" way to proceed without being truly engineered for it.

An innovation pathway, for defining and meeting customer desires in an open innovation frame, was adapted and named by Rebouillat the "Z-process" back in the 90's.

Figure 2 provides the sequences of this process which are self-explanatory. Additional rather common acronyms appear on this flow chart:

- CTQ: Critical To Quality, key measurable characteristics of a product or process
- SWOT: a structured planning method used to evaluate the Strengths, Weaknesses, Opportunities, and Threats
- ATA©: Adjacent Technology Analysis, [1], [2] (Rebouillat & Lapray, 2014; Rebouillat, 2013)
- DOE: Design Of Experiments
- RVA: Rapid Value Assessment complements VOC
- SHEA: Safety Health and Environment Awareness

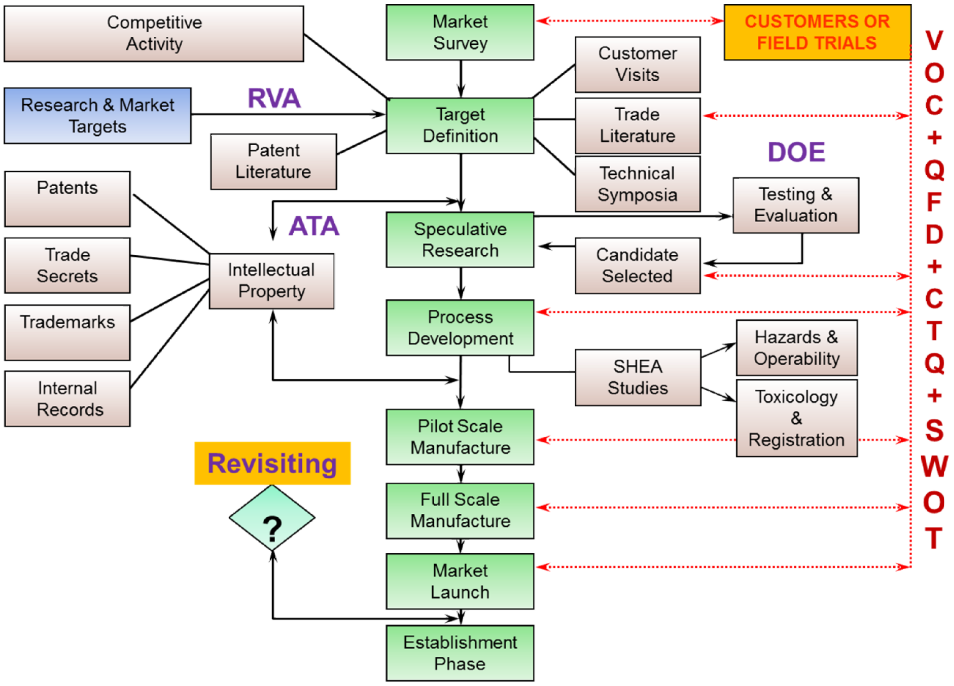


***Figure 2.The Z-Process combines multiple business and technology management processes***

***Patent Quality to "feed" or replace Patent Quantity: a disrupting challenge***

According to "Updating TRIZ: 2006-2008 Patent Research Findings" and adapted figure 3, minor and continuous improvements constitutes about 60% of the average patent portfolio while only 5% are of pioneering/new nature which in turn accounts for more than 70% of the portfolio overall value. Then the majority of the patents accounts for less than 25% of the value of the given portfolio.

The design of figure 3 is disruptive by nature and tough to put in place practically; nonetheless almost paradoxically, quality, emerging from pioneering, has to replace quantity for a broader creativity to happen. This without, at least temporally, hardening the "cash cow" securing cushion, coming from the bulk of the portfolio; that bulk generates a steady profits return that far exceeds the cash needed to purchase or to start it.

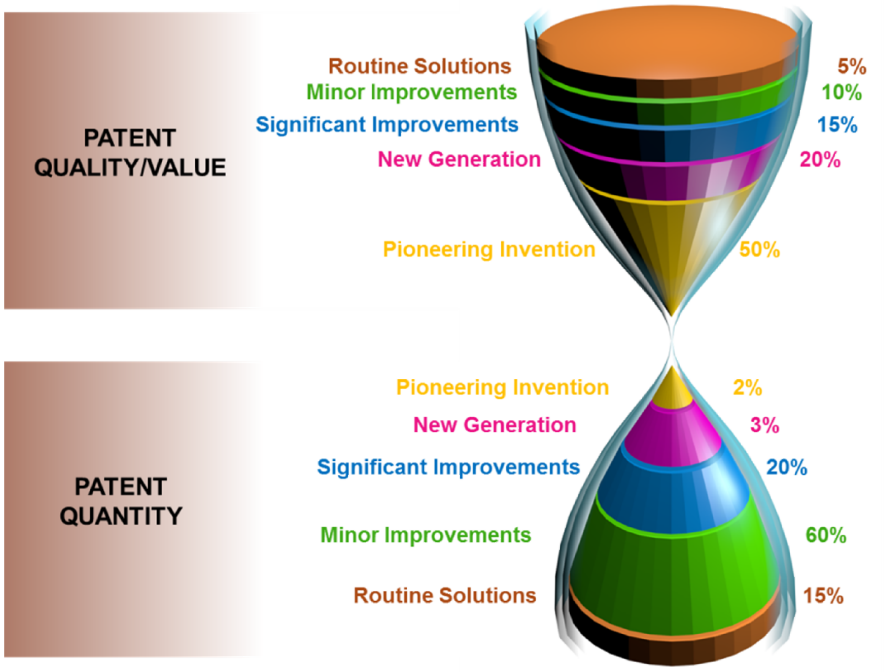


***Figure 3. Electing for Quality maintaining a broad patent "coverage" remains a disruptive challenge***

***Disruptively?***

A disruptive innovation can be a key for the company to prosper and last [4] (Christensen, 1997). The term "disruptive technology" has been commonly used as a substitute of "disruptive innovation". So far, several of such technologies have been inspired by natural environment. In an age of rapidly growing understanding of nature's secret design and concepts we have yet another chapter to add in the story of our joint venture.

***Bio-mimicry vs Biotechnology***

Humanity is continuously inspired by nature and has learned how to use its resources in every domain of life. To do that we often use means of biotechnology. It is the action of using living organisms to develop desired products, using derivatives thereof and modification of organisms (like breeding or genetic manipulation) [5], [6] (Dove, 2000; Thieman & Palladino, 2013).

In addition, in nature we found an inspiration to build planes and fins with capabilities exceeding living creatures. Sometimes, we boldly copy nature solutions, like structure of honeycomb that can be found in, to give just a few examples, LED technology, mirror structure of Hubble telescope, loudspeaker, or various aircraft applications. This is qualitatively different from biotechnology and began the field of bio-mimicry or bio-mimetics (also called biomimesis, bionics or biognosis).

***Wealth of ideas that produce platform of solutions***

The retrieval of all the patents from the US Patent and Trademark Office (USPTO) that contains the keyword "bio-inspired" yields 236 results. Using a recently developed interface to the USPTO to map patent portfolios [7] (Leydesdorff, Kushnir, & Rafols, 2012), we have noticed that documents were clustered around two main areas, namely medical and computational sciences (figure 4). The authors choose then to primarily give an overview of the range of solutions in these two areas. At the same time we do not attempt to describe in depth the underlying technologies, neither to provide an exhaustive list of them. Delivered examples come from all range of categories from those that are in commercial use, ready to be implemented patents and scientific projects that, although promising, still require a great deal of research.

Mimicking nature does not only mean creating a synthetic copy of its solutions. Equally, it can mean that one can look at the solutions that nature provides and be inspired by it. Therefore, in this review terms bio-inspired and bio-mimicking are used interchangeably.

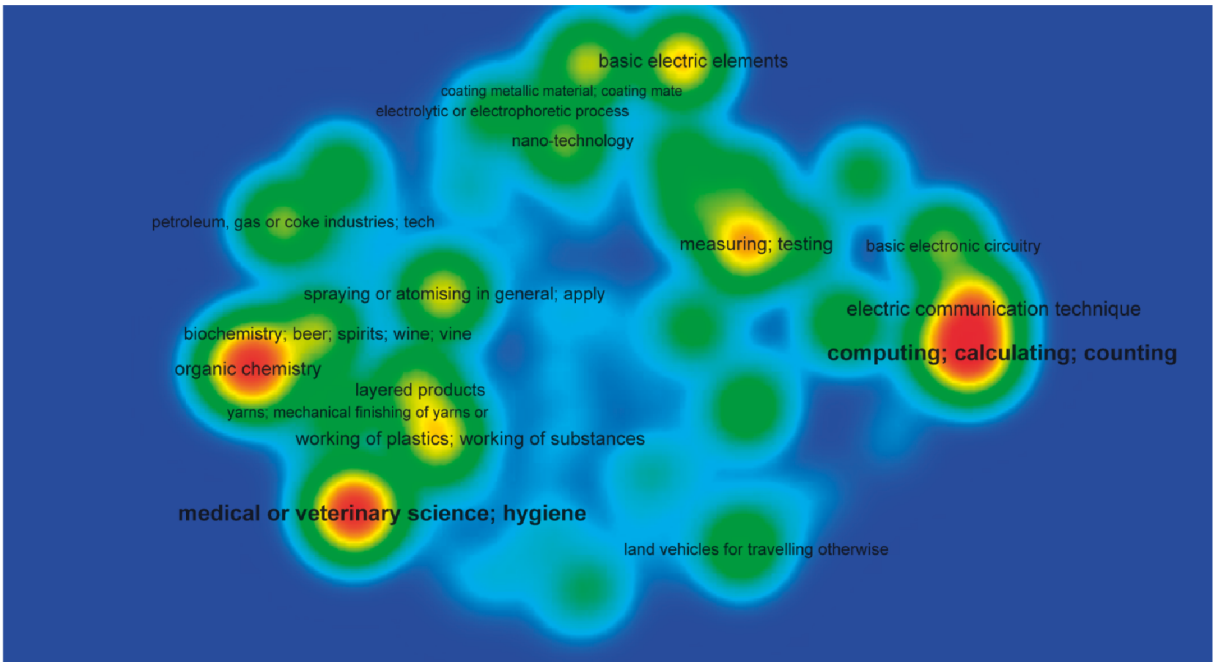


***Figure 4. Mapping of "bio-inspired" USPTO patent portfolios***

Nature mimicking is done on any conceptual level. It can mean rather a straightforward copy of the solution like in the case of Velcro (hook-and-loop fastener) that copies burrs of burdock. Or, can adapt a concept such as behavioural phenomena of animals to create problem solving techniques used in computing [8] (Chakravarthy, Bachan, Roshini, & Chandrasekharan, 2012). Nature "brand" comes with firm promise of solutions that resisted the durability test, have optimal energy consumption and can be simple to implement (provided we sufficiently understand them). It would be unwise to assume though that we can find all the best solutions in Earth environment. Nevertheless, it's a pool of ideas that one cannot neglect.

The solutions provided by nature are applicable to the -nano, -micro, -macro and -mega scale. Moreover, one problem can find several solutions (figure 5). Let's examine the mechanosensing to illustrate that concept by examining nature's product portfolio. The range of possibilities is broad, starting from bacteria and ending in mammalians. Let's turn first to plants, such as the *Mimosa pudica* (common name: touch-me-not) that can react to environmental changes by closing its leaves in less than 0.1s. The basics of that response are simple and relay on a change of inner pressure, so called turgor [9] (Allen, 1969). On the other end of the solutions spectrum we encounter mammalian skin packed with mechanoreceptors connected to neurons. This system allows converting mechanical stimulus (touch, pressure) into an electrical signal further processed by the brain. This ensures great precision of sensation and is crucial to execute fine task of object manipulation [10] (Johansson & Flanagan, 2009). This proposition, although brilliant, is very complex to fully comprehend and therefore mimic. Nevertheless, engineers strive to design prototypes of "sensitive skin" [11] (Lumelsky, Shur, & Wagner, 2001). Perhaps it is satisfactory for one's purpose to look at solutions with less multipart organisation found in insects or spiders, where the majority of sensory information is analysed locally without involving the brain. Sensing vibration is a vital task for spiders as it signals the presence of a prey on the web or a prospective mate. To perform the task, at a level far better than humans, they use "sensory hairs" or so called lyriform slit organs. This system uses deceptive simplicity of sensing changes in air or relevant cuticular strains such as mentioned vibrations [12] (Fratzl & Barth, 2009). Only recently, in-depth analysis of properties of available resources combined with new materials and micro fabrication techniques allowed starting to think about producing synthetic sensors [13] (Johnson, Bonser, & Jeronimidis, 2009).

In a similar manner, it is important to grasp, that many solutions and patents are not applicable to only one described situation as presented below. Many of them comprise rather a platform of solutions that can be used according to one's needs. One example is a technology of self-healing, slippery liquid-infused porous surfaces, abbreviated as SLIPS [14] (Wyss Institute, SLIPS: Slippery Liquid-Infused Porous Surfaces); a material that repels both liquids and solids, which can be used to coat medical devices (as described below) as well as in a rage of different applications. Due to the specification of SLIPS, that can include: (1) transport of crude oil and biofuels; (2) economical heating/cooling systems; (3) ice resistant coatings for devices/instruments operating in refrigerated and polar environments; (4) stain resistant coatings on optical surfaces, such as solar cells, lenses, sensors, and night vision devices; (5) anti-biofouling coatings for medical devices and instruments, and marine vessels, also for deep sea exploration [15] (Wong et al., 2011).

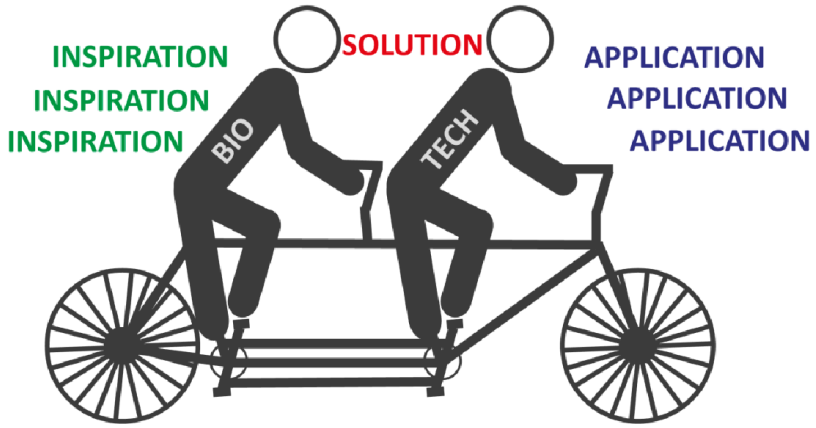


***Figure 5. Platform of bio-inspired solution***

***Biologically inspired technology innovation process and methodology***

The bio-inspired solutions are the result of a meeting, broadly speaking, between biologists and engineers (figure 5). As presented above, the result of such collaboration can produce outcomes beyond our expectations. Nature has uncountable patents, many of them difficult for us to identify straight away. This necessitates novel interdisciplinary approaches starting from the education and training plans that build a bridge between biology and engineering fields. Some efforts in that domain has been already made, an example is the Center for Biologically Inspired Design, a research unit at Georgia Institute of Technology [16] (cbid.gatech.edu). The task of cross domain knowledge translation is not straightforward. The researchers analysed the approach to solve the problem taken by the students with different backgrounds during the course on biologically inspired designs [17] (Vattam, Helms, & Goel, 2007). The study pointed out that biologists and engineers differ in (1) the language they use, (2) the objectives of their work (understanding of the process *vs* creating applicable solution), (3) the complexity of the systems in questions (living organism with variety of simultaneous functions *vs* technical development to master one task), (4) the resources to use (cellulose *vs* steel for reinforcement of high structures) [17] (Vattam et al., 2007). All of those differences were visible during the execution of the projects and resulted in frequent cognitive errors such as issues in defining the problem with appropriate level of specificity and not being able to create correct analogies [17] (Vattam et al., 2007). The authors proposed to use interactive computational tools to facilitate the process of innovation by retrieving the relevant biological information for given technical problems [17] (Vattam et al., 2007). It seems that creating a library and tools that could create appropriate analogies to link biology and technology is a promising approach. Some propose to take into account the complexity of living organisms in question and focus not only on physical properties but also on environment, the cause and purpose of action, available resources and auxiliary systems involved [18] (J. F. V. Vincent, Bogatyreva, Pahl, Bogatyrev, & Bowyer, 2005). Nevertheless, we must remember that we need to reach a deeper understanding of differences in the approach between man and nature to solve similar issues, and some initial data point that they are substantial [19] (J. F. V. Vincent, 2005). In addition, there is a key challenge in front of us of how to make the process of bio-inspired innovation more systematic, and not of retrospective in approach.

In essence, an algorithm to structure methodology in technical innovation exists (like one known as TRIZ) and some think that, if transformed to match a bio-setting, may prove to be a useful procedure. Russian inventor Genrich Altshuller analysed hundreds of thousands of patents and that allowed uncovering patterns of evolution for technical inventions. This set of observation was a foundation to develop rules describing a systematic process to solving technical problems, known as TRIZ (acronym from Russian name) or referred as "the theory of inventive problem solving" [20] (Altshuller, 1999). TRIZ algorithm became worldwide recognised tool and many Fortune 500 companies successfully use its methodology [21][1]. The general TRIZ principles of transfer of functions, mechanisms and principles from one field to another are very similar to the process of bio-mimetic. Therefore, some tried to examine its usefulness in a new field. The problem in TRIZ terminology is defined as a conflict between two contradictory elements, e.g. when the product needs to be stronger but can't be heavier. Based on patent analysis, all contradictions were classified in a form of 40 Inventive Principles. Every conflicting element was next considered according to a list of 39 factors, which in addition could impact on each other. The result of such combination generates a contradiction matrix of functional problems. It helps to identify and narrow the problem and in a next step can provide a method for resolution based on ways in which similar problems have been resolved by other people, often in other areas of science and technology. The key is to sufficiently generalize the conflict to allow insights from a variety of disciplines, that in turn increases the possibility to generate more innovative solutions [20] (Altshuller, 1999). Since, it is difficult to apply a common "language" applicable for both biology and technology, the first step was to examine a few case study examples from nature trying to recognise solutions to contradiction-like problems and examine whether the 40 Inventive Principles apply [22] (Mann, 1999). From the gathered data, mostly from macro-scale cases, it appears that Inventive Principles could be used but the ability of the current Matrix to mimic natural inventions is small [22] (Mann, 1999). Analysis of arthropod cuticle is another example of thorough attempt to translate biological functional design in terms of standard TRIZ Inventive Principles [19] (J. F. V. Vincent, 2005). The authors identified the functional conflicts and looked at the solutions proposed by nature and technology, it turned out they were overlaying in about 20% [19] (J. F. V. Vincent, 2005). Authors suggested that this mismatch may be a derivative of several factors. Firstly, it is essential to consider a living system in a context of its environment, and not, as in the case of technology, in isolation. It is necessary to identify what are the components that create the system under consideration, as well as to what higher in hierarchy system it belongs to. In case of a specific tissue, taken as an example, it is helpful to recognise what cell types it is built of and what organ it will create. In turn, it will help us to understand the purpose of action, causes, limits and effects of a system. This initial consideration and definition of the system can help to identify if such a function is even described in the TRIZ system or needs to be added as another possibility. Next, we must carefully consider what resources were available when the biological system was created as it is a key determinant of its development. Finally, since the living systems are embedded in hierarchical structures, several auxiliary elements can be involved in execution of its function. Complex interaction between units of natural ensemble will most likely cause unpredictable effects. Further studies, by the same group, confirmed and further demonstrated that technology and biology employ different strategies to solve the same problem and that we can benefit from looking into nature's design to uncover a surprising result [23], [24] (Bogatyrev & Bogatyreva; J. F. V Vincent, Bogatyreva, Bogatyrev, Bowyer, & Pahl, 2006).

Having an indication that biologically inspired technology carries uncovered potential it would be unwise to abandon this new engineering domain. Although we are still struggling to design a systemic approach to generate innovation in bionics domain we should keep up our efforts as even in the current environment they bring measurable results. At the moment, the development of bio-inspired-technology is powered by knowledge generation lead by inter-disciplinary studies and continuous dialog between engineers and biologists. The growth of innovation inspired by nature is a derivative of gathered knowledge described in a common for all interested parties language (figure 6).

[1] *www.aitriz.org/triz*

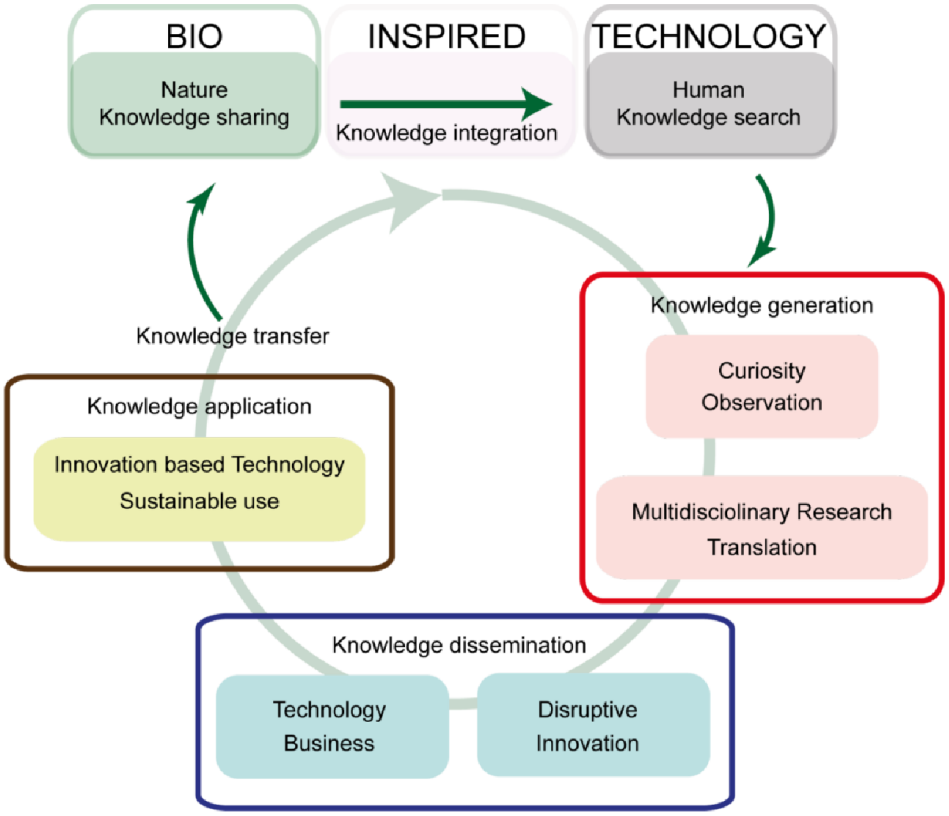


***Figure 6. Knowledge flow***

## 2 BIO-MIMICKING - FUTURE INNOVATION DRIVE FOR PHARMACEUTICAL INDUSTRY?

The pharmaceutical industry is clearly one of the most innovation demanding ones [25] (IFPMA, 2013) and as such can clearly benefit from a bio-mimicking approach. It became extremely important since the rate of truly new drugs being launched is decreasing in recent years [26] (Pammolli, Magazzini, & Riccaboni, 2011). We present below some of the new developments that may become disruptive innovation for the industry.

***DNA-based nanostructures as targeted drug delivery systems***

DNA is a biological material that stores, codes and transfers information. Due to its properties of self-recognition and self-assembling it has been used to create nanostructures that can serve different functions. It is an interesting example of bio-mimicry where scientists are deliberately taking advantage of the properties of natural polymer to create structures with purposes not foreseen in organisms but desired by bioengineers.

The area of structural DNA nanotechnology uses a technique called DNA origami, where a long piece of DNA strand is folded into a desired shape with hundreds of short staple strands [27], [28] (Rothemund, 2006; Yan, Labean, Feng, & Reif, 2003). This relatively new technique (pioneered in 2006) allowed creating three-dimensional and polyhedral structures with desired, pre-defined shapes and dimensions in nano-scale not achievable beforehand.

The DNA nanostructures possess a combination of features that allows us to consider them as system for drug delivery. Firstly, and somehow obviously, they are bio-molecules and as such they are compatible with bio-systems [29] (Ko, Liu, Chen, & Mao, 2008). Therefore, there are little associated threats of its accumulation and/or toxicity like in the case of inorganic or artificial nano-materials, however certain shapes may have some immunicity [30] (Origami et al., 2011).

Crucially, unlike nucleic acids they can cross cells membrane [29], [31]–[33] (Hamblin, Carneiro, Fakhoury, Bujold, & Sleiman, 2012; Ko et al., 2008; Li et al., 2011; Walsh et al., 2011). It has been suggested that just certain geometry could be sufficient for the nano-structure to be internalized by a cell [31], [32] (Hamblin et al., 2012; Li et al., 2011). In that context

being able to produce specific shape is fundamental. Lastly, they prove to be stable in physiological conditions after internalization [31], [32] (Hamblin et al., 2012; Li et al., 2011). In addition, there are several methods that allow the coupling of DNA nano-structures with active compounds, these include small molecules, nucleic acid, proteins and other nano-particles [34] (Li, Fan, Pei, Shi, & Huang, 2013).

Influenced by these advances Douglas and colleagues designed a DNA nanorobot capable of delivering signalling molecules to selective cell population [35] (Douglas, Bachelet, & Church, 2012). It is an important point as currently we are designing drugs (ligands) to act on their selective targets. The latter are most likely present in many places of biological systems and activated cause widespread, additional to therapeutic, unwanted side effects.

The designed nanorobot has a form of hexagonal barrel that consist of two domains attached to each other. Next, they designed two "lock" mechanisms that open when binding to "keys"; they were added in front of the barrel, on left and right side. When both locks recognise their target they open (dissociate) and initiate a reconfiguration of the barrel (it halves). This exposes previously hidden surface with attached cargo (that can carry up to 12 payloads). Only when the robot simultaneously encounter a correct combination of keys it will become active, and there is no competitive mechanism that could open it. In inactive state (closed barrel) the cargo cannot interact with cells. The authors showed that several cell lines could selectively activate the robots, up to the single-cell level. Importantly, the nanorobot was shown to discriminate target cell types (derived from granular lymphocytic leukaemia, aggressive natural killer cell type) in a mixture with healthy leucocytes. Finally, activated nanorobots induced growth arrest in the above cell line [35] (Douglas et al., 2012).

To sum up all of the above, it opens up a possibility of a new era of effective, cell population oriented drug delivery system with possible low side effects, and creates wealth of possible interactions of inorganic particles with biological systems.

In a similar manner, the self-assembly properties of DNA was used to create complex structures that coat inorganic nanoparticles (used as therapeutics, contrast agents and integrated systems for treatment and diagnosis of disease). As mentioned beforehand, such a strategy was designed because, despite their effectiveness [36], [37] (Park et al., 2010; Perrault, Walkey, Jennings, Fischer, & Chan, 2009) they are not well cleared from the body and such a persistent presence in the system may lead to a variety of toxic effects. Therefore, to counteract that unwanted effect several studies tried to improve the process of drug delivery and elimination by combining inorganic particles with organic molecules. The recently proposed structure consists of a central (core) nanoparticle surrounded by DNA with a possibility to add several layers of additional particles surrounded by DNA with different sequences that insert themselves into the previous layer [38] (Chou, Zagorovsky, & Chan, 2014). The final DNA coat is covered with additional ligands that enable interaction with biological systems. It has been shown that superstructures after entering the system can specifically accumulate in tumours (without non-tolerable side effects) and be effectively eliminated by kidneys [38] (Chou et al., 2014). Altogether this allows designing diversity of colloidal superstructures that can serve as a drug delivery platform with desired biological stability, low and non-specific interactions with biomolecules and cells and favourable pharmacokinetics.

Both examples open doors to a whole class of novel enabling technologies that uses DNA as building material, with potentially very big impacts.

***Bio-inspired solutions for R&D cost saving***

The cost and time of successfully launching a new drug on the market is ever growing, reaching USD 1.3 billion and lasting over 14 years [25] (IFPMA, 2013). In that process the numbers bluntly point out that more and more substances do not reach or pass subsequent clinical trials that translate to higher costs. Some of that can be reduced by more rigorous fundamental and pre-clinical research of new molecular entity that subsequently have higher chances of success and launch [39] (Paul et al., 2010). Can some of the bio-inspired technologies contribute to investments saving during the R&D process?

We are not yet able to simulate the complex physiology of an organism; therefore the use of animals during final elucidation of an impact of tested new molecule on biological networks cannot be replaced. Unfortunately, in addition to other disadvantages, we have very few reliable animal models of disease and the results of such studies not necessarily translate to human. At the moment, initial data collection concerning the action of new molecules is performed in living cell cultures. This gives rather limited insights as concerns single cells type and a result excludes further tissue, organ and system level interactions. Both issues can be overcome with the possible use of "organs-on-chips" that can both give insights into system levels actions of tested molecules and reduce the use of animals [40] (Huh et al., 2013). The idea is to culture living cells in micro-channels (polymeric or glass) that express and maintain tissue specific functions. Examples include most of human cells from brain, kidney, liver, heart, skeletal muscle and intestine. Recently improved systems mimic chemical and

mechanical environment of human organs and allow tissue to tissue interfaces. With the use of these systems one can truly mimic physical and chemical environment and thus organ level function [40] (Huh et al., 2013). As a proof of concept lung-on-chips have been used to predict efficacy and toxicity of new therapeutics against pulmonary edema [41] (Huh et al., 2012). This can become a future approach to test drug efficacy and safety in pharmaceutical as well as fundamental research context.

Finally, one could think of increasing the effectiveness of producing biopharmaceuticals taking a closer look on natural systems self-regulation. Mimicking of the ecosystems provides a proposition of bio-supportive medium with at least one nutritional and bio-limiting agent [42] (Guritza, 2003). Specific configuration of such an artificial environment can enhance production of active pharmaceutical compounds. Bio-inspired medium is also another example of multiple application of one technology solution (figure 5). It could be used to limiting growth of unwanted bio-mass on materials exposed to aquatic environments. It is an alternative to currently used coatings that prevents bio-fouling and corrosion, but often includes toxins, therefore their use is limited.

The above section 2 related to the pharmaceutical industry has been subject to semantic analysis performed by two different search engines, and then clustering. The study was performed on the first 1000 most relevant patent references for the sake of processing ease. Obviously the two searches converge as per comparison of the left and the right gearwheels clusters on figure 7.

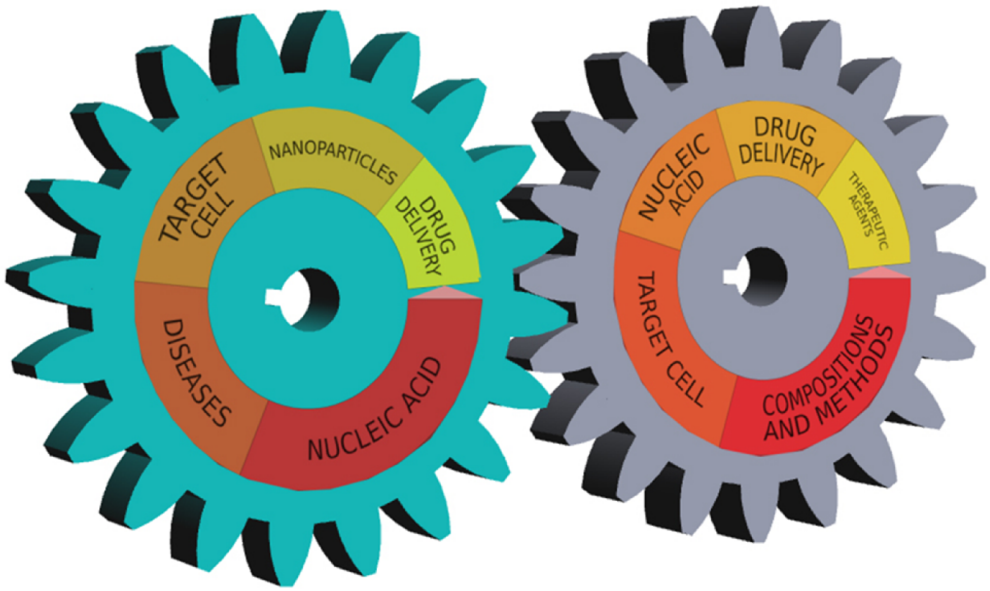


***Figure 7. Semantic analysis and clustering of section 2 – "Pharmaceutical Industry"***

## 3 BIO-INSPIRED MATERIALS, TECHNIQUES AND TREATMENTS IN MEDICINE

Similar to pharmaceutical industry, biologically inspired solutions in the area of materials, technical devices or treatments have the capability of pushing the frontiers of medicine as we know it. Several examples presented below, although apparently not related to each other, will help to shape a bigger picture.

We will not be soon capable of mimicking the precise hands movement of a surgeon. In fact, even manipulating delicate materials, including human tissue, by machines is a challenging task. Engineers found an inspiration in a simple feeding apparatus mechanism of molluscs (like California sea slug). It is a muscular structure that is able to grasp and move food into the animal's body. The invention is mimicking this specific muscular arrangement and its capability of gripping and manipulating fragile, irregular materials in the lumen. It can be complemented by sensors to detect local environment changes e.g. in pressure and can be manipulated *via* external control systems. The above technology therefore could be used in, among many, medical applications such as removing plaque from blood vessels [43] (Hillel, Beer, Mangan, Quinn, & Sutton, 2010).

Deposit of plaques (cholesterol) obstructs arterial blood flow, and will most likely lead to the development of cardiovascular diseases. These are the most common causes of death and in the same time become a financial burden for the society [44] (American Heart Association, 2013). To keep arteries open, surgeons insert bare metal mesh tubes, called stents. This solution is not perfect and patients can suffer from re-closure of the artery. It can be initiated by stents themselves that penetrates into the vessel wall. The interior surface of blood and lymphatic vessels consist of thin layer of cells called endothelium. It forms an interface between circulating blood or lymph in the lumen and the rest of the vessel wall. Its function is far more complex than just a barrier and includes control over blood pressure, inflammation, release of agents against blood clotting and supporting formation of new vessels, as well as repair of damaged organs. Disruption of the endothelium function can lead to the cascade of events resulting in serious complication. Therefore, stents have been equipped with drug eluting coats; sadly they did not manage to solve the entire problem. Alternatively, one could think of mimicking original endothelium cell layer to avoid the above problems. Recently, a natural endothelium mimicking nanomatrix that could be used to coat medical devices such as vascular stents has been patented [45] (Jun, Kushwaha, Brott, & Anderson, 2010). It uses peptide-based molecules that self-assemble into nanofibers, so called peptide amphiphiles, which host endothelial cells [45] (Jun et al., 2010). The aim is to simulate natural cells environment, so called extracellular matrix (ECM). Extracellular matrix, although variable in types, can be described as surrounding of the cells that provides multiple functions. This includes structural support, cell-to-cell communication, adhesion and complex signalling involved in cell growth or healing. Another example approach to mimic such conditions is the use of cellulose acetate porous membrane (that can also comprise carbon nanotubes) [46] (Gouma, 2007). In this case, artificial scaffolding from natural polymers could be used in the process of tissue bioengineering for therapeutic purposes such as custom-made skin implants. Which of the two patented approaches can prove to be more compatible with our organism is yet to be determined.

In our imagination, hospital is associated with an almost sterile place. It is self-explanatory why maintaining a clean medical environment and tolls is a necessity. Novel materials can help with achieving this labours task. Engineers were inspired by the Nepenthesis pitcher plant that has very slippery surface crucial for catching a prey. The rim of the plant has a microstructure that locks-in liquids and then acts as a repellent surface. Insects with drops of water on their feet that step on it then slide straight to the digestive juices of the plant. This idea led to the design of a synthetic material called: self-healing, slippery liquid-infused porous surfaces, or SLIPS [15], [47] (Aizenberg, Hatton, Ingberg, Super, & Wong, 2012; Wong et al., 2011). SLIPS are able to repel a broad range of liquids such as oil or blood making it the perfect coating for a variety of applications.

Prevention is better than treatment in every aspect under consideration. In everyday life it proves to be challenging to maintain good posture while sitting on an office chair and working for long hours. Engineers patented a system that employs mimicking of human body posture to help keeping a healthy position during work as well as during correlated discrete movements [48] (Tholkes & Hockenberry, 2004).

Finally, an example of a futuristic treatment for impaired vision inspired by primitive water organisms. This story is about a multi-layer example of bio-inspired technology and concepts and will slowly reveal its potential in the next paragraphs.

The green alga (*Chlamydomonas reinhardtii*) is a well-known organism in the biopharmaceuticals and the biofuel field as a source of hydrogen. However we are particularly interested here in how this single cell organism is able to move in response to, and towards light. The light is detected by a family of proteins that serves as sensory photoreceptors, so called channelrhodopsins (ChR; figure 8). In practice, they form a passage (channel) connecting the inside of the cell to the external environment. It can be either open, when it absorbs light, or close. ChR absorbs blue light that results in a change in the anatomy of the protein that opens up and allows the free flow of ions (cations such as $H^+$, $Na^+$, $K^+$, and $Ca^{2+}$). In turn, movement of electrically charge ions changes a cell's potential across the membrane leading to its activation or inhibition. In other words, one could say that ChR forms light-gated ion channels [49] (Kato et al., 2012).

Ion channels are present in all cells and they shape electrical signals by gating the flow of ions across the membrane. This is no different to specialised brain cells, neurons. However, they are a key component of neurons physiology as information in the brain is processed and transmitted through electrical and chemical signals. It is not surprising that the voltage gradients across neuron membrane are maintained by a combination of ion pumps and ion channels. Together, this led to the idea of controlling activity of brain cells by inserting into their membrane the green algae ChRs and manipulating them with light (figure 8). Now the last task at hand is how to insert them and gain full control of ChRs and therefore neurons?

With the current techniques it is rather a straightforward task. Scientists have at hand a variety of transfection techniques (viral transfection, electroporation, gene gun) that force neurons to express and integrate ChRs into their membrane. Important to note that such cell modification, in principle, does not lead to any signs of toxicity.

One needs to add, that we can not only activate neurons with the blue-light sensitive ChR but also silence them with yellow light-activated chloride pump halorhodopsin, from *Halobacteria*. The field of controlling genetically modified cells with light has been termed optogenetics [50] (Deisseroth, 2010).

The repertoire of multiple-colour optical activation with millisecond precision is heavily used to probe the function of nervous system [51] (Deisseroth, 2011). However, first efforts have been made to use it as a therapeutically valid tool.

These bring us back to our main point of applying optogenetics to a problem of vision degeneration. The inner surface of the eye is a light-sensitive layer of tissue, and its degeneration leads to blindness [52] (Lagali et al., 2008). The photosensitivity is ensured by photoreceptors coupled to neurons that relay the information to the cortex of the brain that will "analyse" the image. In the situation when photoreceptors have been lost inserting ChR2 to retinal neurons could lead to their excitement by light (figure 8). Indeed, inserting light sensitive channels to specific cell types (called ON bipolar cells) in a mouse model of disease restored some signalling towards the visual cortex and was sufficient for the animal to perform given tasks [52] (Lagali et al., 2008). These results hold a promise that this technique will be applicable to the treatment of other neurological diseases that necessitate cell-specific modulation.

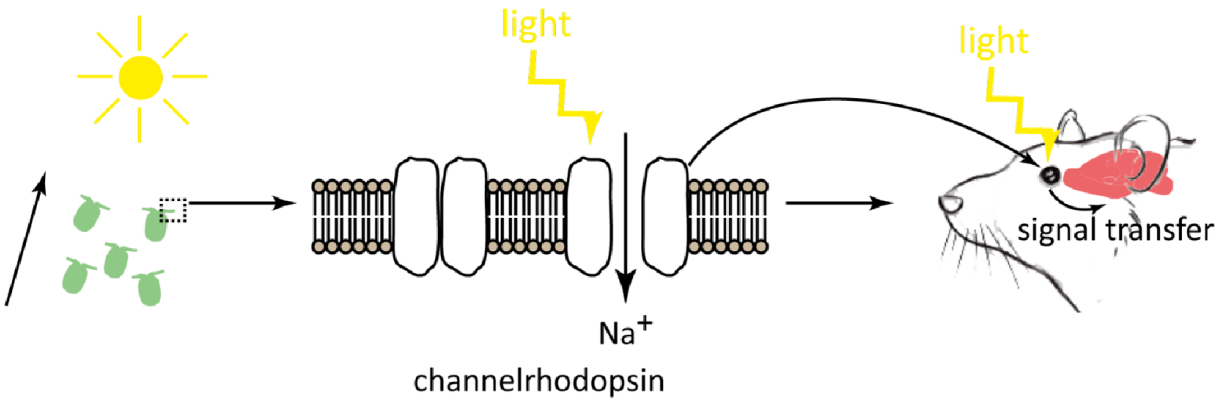


***Figure 8. Optogenetic-based treatment vision degeneration***

## 4 HOW WE PATENT SOLUTIONS PROVIDED BY NATURE FOR PHARMA/MEDICAL TECHNOLOGIES?

Currently solutions developed by nature are (mostly) not protected by patents. One can have easy web access to genome database of several animals e.g. bacteria E. Coli [53][2] and human [54][3]. The above was re-enforced by a decision of U.S. Supreme Court (on June 13, 2013, in Association for Molecular Pathology v. Myriad Genetics, No. 12-398), that unanimously ruled that, a naturally occurring DNA segment is a product of nature and not patent eligible merely because it has been isolated [55] (Ledford, 2013). It is an important decision because since 1980, the USPTO granted patents on more than 35,000 gene sequences (20% of human genome). This decision invalidates Myriad's patents on the markers for breast and ovarian cancer: BRCA1 and BRCA2 genes. In practice it means that other companies will be able to propose the test detecting mutation of the above genes, which will most likely result in a cheaper price for this service and will become more accessible to women. On the other hand, removing the protection of intellectual property, crucial for commercial investment, can slow down the development of new products or may push companies to protect inventions as undisclosed trade secrets. Importantly, the court also held that manipulation of a gene to create synthetically-produced complementary DNA could still be eligible for patent protection. This statement has already caused confusion as there is no further guidance to determine how much modification is sufficient to justify a patent. The same question is currently under revision considering the stem

[2] *www.genome.wisc.edu*
[3] *www.doegenomes.org*

cells research [56] (Marshall, 2014). An advocacy group (Consumer Watchdog) aims to invalidate a patent from 2006 awarded to biologist James Thomson, who was the first to isolate and culture stem cells from human embryos [57] (Thomas, 2006). The implications of withdrawing a patent, both for public sector research institution and commercial technology transfer are not straightforward to predict [58] (Bergman & Graff, 2007). Clearly, this uneasy and vital discussion has just been opened.

## 5 BIOLOGICALLY INSPIRED SOFTWARE AND HARDWARE – A WAY TO SOLVE EVERY COMPLEX PROBLEM?

Some problem cannot be simply solved using rule-based software code. This is when we turned to nature to look for ideas to develop algorithms to help us. Insights into how biology manages complex matters of structure, behaviour and operation of systems and organisms have proven to be a fruitful source of stimulation. Depending on the specific source of inspiration, algorithms can be further divided into several categories: (1) artificial neural networks inspired by animals' central nervous systems; (2) evolutionary algorithms (EA; including genetic algorithms, GA) that use mechanisms inspired by evolution; (3) swarm intelligence (SI) that attempts to mimic the behaviour of a group of independent organisms such as ant or bee colonies, bird flocking, wolf group hierarchy, bacterial growth, etc.; (4) others. It is virtually impossible to discuss here in depth all available tools, their structure and application, and it's not our primary goal. It is nevertheless important to emphasise that all of them can be used to solve a variety of problems in fields such as financial modelling [59] (Brabazon & O'Neil, 2010) or computer networking [60] (Meisel, Pappas, & Zhang, 2010).

Human brains are highly plastic, process information in parallel, learn easily, use semantic interpretation of speech, process image and solve many more conceptual problems. It is therefore our ultimate inspiration to design some of those desirable characteristics. It seems that the key element allowing a brain to outperform computers in many tasks lies in their system architecture build from a variety of extremely interconnected processing units [61] (Buzsaki, 2006). The basic hardware unit of the brain super computer is the single nerve cell, called neuron (figure 9) [62] (Hammond, 2008). These are excitable cells. When they receive relevant information they generate electrical signals and propagate them along their processes (called axons and dendrites). This capacity is due to the presence of proteins in their membranes which allow the selective passage of ions, called simply the ion channels. These are similar to channelrhodopsins, mentioned in a previous chapter, with the difference that they are activated by a change in membrane voltage, not a light. Neurons generate only one type of electrical signal called an action potential (AP) or a spike. Moreover it is "all or nothing", 0 or 1 type of signal, it can simply occur or not. The details of information it carries are therefore coded in the frequency of neuronal discharge. Neurons are not (mostly) connected by membranes, so that electrical signal cannot freely propagate from one to another. Instead they communicate by specialised zones of contact formed between cells that are called synapses. They are specialised in the transmission of information in chemical form and although slower, they contain a myriad of information compared to an electrical signal. Such a communication is possible because neurons are also secretory cells. The product that they release is called neurotransmitter, and can be any small molecule like amino acids, peptides, or monoamines. After an AP reaches the restricted membrane part of the neuron (synapse) it signals the release of neurotransmitters to the extracellular space. Next, the chemicals bind to and subsequently activate ion channels present on the membrane of the receiving neuron. In turn, opening of channels may initiate AP and signal transmission in the receiving neuron [62] (Hammond, 2008).

Based on those principles, an artificial neural network can be already modelled. It uses artificial nodes, equivalents of neurons, that are connected together to form a network (figure 9). The artificial synapse is assigned a strength or amplitude of a connection between two nodes, and is known as synaptic weight. Artificial neurons are simplified, mathematical models of biological equivalents described above [63] (McCulloch & Pitts, 1943). McCulloch-Pitts model of neuron has many inputs (i.e., analogue of dendrites, post-synaptic site of network) with attributed weight (w) and one output (analogue of axon, pre-synaptic site of network) [63] (McCulloch & Pitts, 1943). Similar to its natural counterpart, the output vector value (of 1 or 0) next propagates to the input of the next artificial neuron, through a synapse. Similar to its natural process, the weight of artificial synapse, and hence the connection between units is changing during learning. This simplistic analogy is sufficient to give artificial network biological properties such as the ability to acquire knowledge through learning and storing information within inter-neuron connections. The artificial neurons can be connected in series; in so-called feed-forward networks (figure 9). If nodes have internal loops (or feedback connections) then their architecture is referred as recurrent network. The objective of every neural network is to transform the inputs into meaningful outputs. And again, the key factor to determine signal processing is the architecture of the network. The most common neural network, belonging to feed-forward family type, is the multilayer perceptron. The multilayer perceptron can produce only one set of output values because artificial neurons are organised into layers that are nonreciprocally connected (this is a so-called static system). On the other hand, the recurrent network is equipped with feedback paths that allow a modification of subsequent inputs to the nodes (this is a so-called dynamic system) [64] (Jain, Mao, & Mohiuddin, 1996). The true power and advantage of neural networks lies in

their ability to learn. Briefly, the network is adjusting the weight between nodes during the training process. It is able to derive them directly from the given examples and improve them after several repetitions [64] (Jain et al., 1996).

Generally speaking, this is a point where analogies with biology to create software's based on artificial neural networks has been replaced by methods of statistics and signal processing. Let's examine the next step that would be interesting to model and add to artificial neural network – that is considering two types of neuron. Depending on the action of neurotransmitters, released by a synaptic ending, we can divide them into one that will excite/activate the receiving (post-synaptic) neuron or will inhibit/stop the generation of spike. Differentiation between excitatory (E) and inhibitory (I) neurons is a crucial point. Natural networks composed of only excitatory units (as it is the case for artificial neuron) is extremely unstable and produces simple and predictable results. Excitation will lead to excitation at every step, resulting in ever-growing increase of activity, exhaustion and shut down of the network (figure 9). It implies that the network requires a control system to be able to carry out useful information. In contrast, when you introduce inhibitory units into the chain, its activation will supress the discharge of its target neuron [65] (Pouille & Scanziani, 2001). Depending on the target type it will inversely influence the network. These differences in the behaviour of two types of chains of neurons are further illustrated on figure 5. In the second configuration, resembling natural system, it is more difficult to predict the spread of the input and activity of every unit as it strongly relies on the details of the connections. In other words, this network generates nonlinear effects and complex behaviours [66], [67] (Dupret, O'Neill, & Csicsvari, 2013; Lapray et al., 2012).

To sum up, the true complexity of the brain's operations emerges from the relationship of interacting elements, and the activity that can be transmitted in both bottom-up and top-down directions. Modelling such complex network and its behaviour with the use of software tools has its limits. Therefore, some researchers are trying to build hardware realisations of spiking neurons models and networks. To build a silicon analogue of a biological neuron, one needs to mimic the behaviour of a cell determined by, described above, voltage-, ion-, and neurotransmitter triggered conductances. It can be done by representing neuronal membrane as electrical circuit's equivalent. In electrical circuit, a membrane is a capacitor and ion flows are represented as leak conductance. It has been manufactured by using a combination of complementary metal-oxide-semiconductors circuits. Importantly, a silicon neuron, modelled on a cortical principal cell, would respond to applied stimulus in a similar way as its biological counterpart [68] (Mahowald & Douglas, 1991). This approach truly mimics the properties of a biological tissue rather than interpreting its principles to create artificial networks. This qualitative difference may bring us closer to create machines more suitable to solve real world problems. An example to support that notion comes from a neuromorphic hardware [69][4], which successfully executed algorithms that classify data with different features [70] (Schmuker, Pfeil, & Nawrot, 2014). Importantly, this approach takes into account the natural variability in morphology and function of the brain and includes processes such as lateral inhibition [70] (Schmuker et al., 2014).

[4] *www.kip.uniheidelberg.de/cms/vision/projects/facets/neuromorphic_hardware/single_chip_system/the_spikey_chip/*

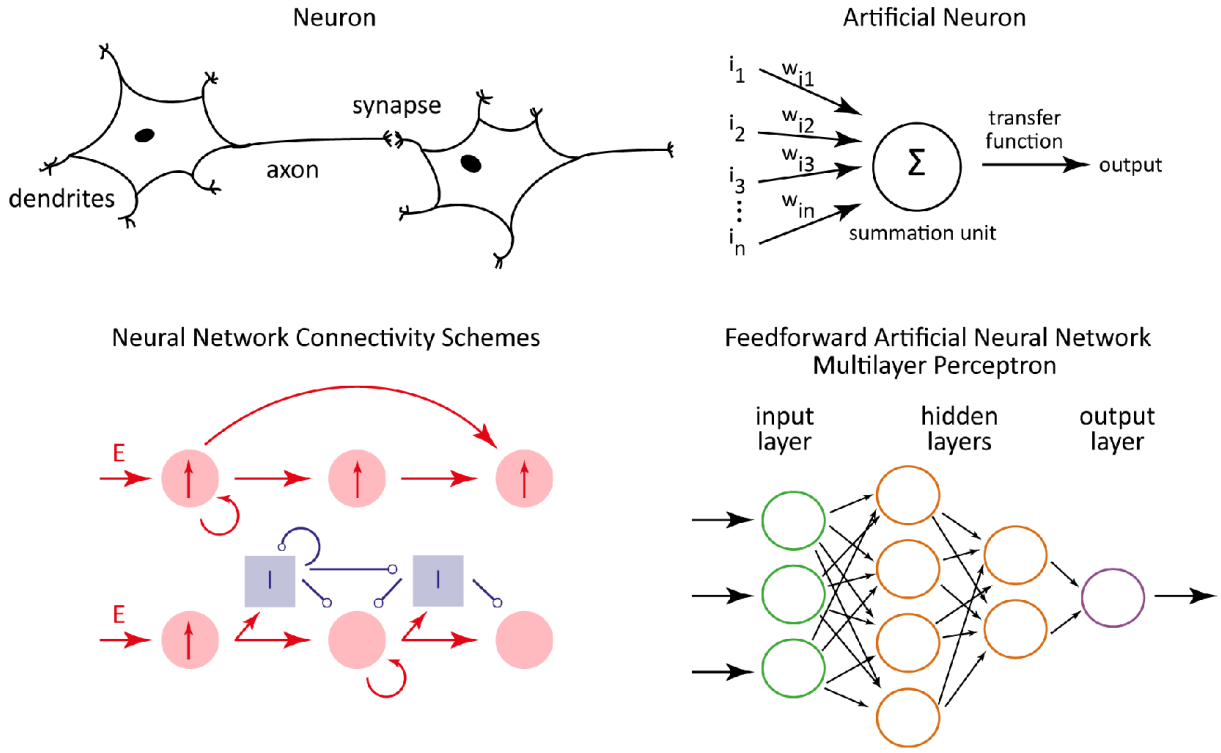


***Figure 9. Natural vs artificial neuronal networks***

## 6 WILL BIO-INSPIRED INNOVATIONS CHANGE OUR FUTURE ENERGY SOURCE?

We are facing an increase in demand for energy accompanied by higher emission of $CO_2$ and fast depletion of fossil fuels reservoir [71][5]. There is an immense need for improvement in harvesting, transformation, delivery and the use of energy today. In nature we found several models that could help us in that challenge. In the centre of attention is the process of photosynthesis. It is an immensely important one for our ecosystem chain of reaction that converts sunlight into chemical fuels in the form of chemical bonds (as a storage system). The prospect of using free and enormous resources of solar energy that every day reaches Earth seems to be a perfect solution. However, the natural photosynthetic process is characterised by a low efficiency of 0.1% to 8% and as such can't be used directly. It applies both to photovoltaic electricity (solar cells) and the production of biofuels from biomass. One of the plausible strategies for producing sustainable fuels would be to create an artificial process of photosynthesis. The goal being to mimic the process of translating bioenergy to fuel with the use of much more efficient and simpler technologies than nature's, as well as to be able to scale it up at reasonable cost to meet our demands. There are growing efforts to bring interdisciplinary scientists to encounter the challenge [72][6] and raise awareness among industry and policymakers of benefits of solar fuel use [73] (Royal Society of Chemistry, 2012).

Before turning to specific examples, the reader can benefit from going a bit more in detail of how the process of photosynthesis works in green parts of plants, algae and some bacteria. It will facilitate our understanding of which elements we need to reproduce. In the big picture a plant simply uptakes water through its roots and carbon dioxide ($CO_2$) through leaves and with the use of light it produces glucose (substrate for respiration and building material) and oxygen ($O_2$), see figure 10. Behind the curtain a complex process of converting light energy to chemical energy takes place in specialised organelles called chloroplasts. This is where the main player, one of few known photosynthetic pigments called chlorophyll

[5] *www.worldenergyoutlook.org*
[6] *www.lbl.gov/LBL-Programs/helios-serc/html/overview.html*

captures the energy from the sunlight. Chlorophyll absorbs light in the blue and red portion of the electromagnetic spectrum, and reflects green and near-green portions of the spectrum; therefore the leaves of the plants (chlorophyll-containing tissues) appear to be green. All chloroplasts have at least three membrane systems; one of them is the thylakoid system, that floats in a semi-gel-like fluid called stroma. The energy conversion takes place on that membrane as it is enriched in green chlorophyll molecules arranged in and around photosystems. As the term photosynthesis itself suggests the process has two steps. The first part, -photo, necessitates light and takes place on the membrane of thylakoids and the second part, -synthesis, is light independent and takes place in the stroma, and is called the Calvin cycle. In the broad view, during the photo- part light delivers energy necessary to split the water and that will eventually lead to producing NADPH and ATP (high energy biological fuel) and $O_2$ (considered here as waste product and responsible for the Earth's atmosphere). Light is powering the movement of electrons, extracted from water, through the electron transport chain. This movement causes the protons to go inside the thylakoid and creates a positive charge. The protons move out through one available channel created by a protein called ATP-synthase. As a result NADPH and ATP are now in the stroma and are ready to be incorporated in the next Calvin cycle. Their role is to supply energy that will allow incorporating carbon from $CO_2$ and synthesising various sugars such as glucose.

Our aim is to target two reactions: the light driven splitting of water into its component parts hydrogen and oxygen, and the light-driven reduction of $CO_2$ by water to give CO, oxygenates or hydrocarbons. The successful design of a chemical strategy to deliver the latter is a grand challenge which has not yet been effectively prosecuted. The process of artificial photosynthesis can terminate with the formation of $H_2$ or carbon-based products (e.g. methanol or methane). The stoichiometry of water splitting into molecular oxygen, protons, and electrons is deceptively simple; achieving it by chemical catalysis has proven remarkably difficult. Many approaches have been adopted with variable success [74] (Andreiadis, Chavarot-Kerlidou, Fontecave, & Artero, 2011). For instance in 2011 Andreiadis and co-workers created a triad assembly that could mimic the three steps of the natural photosynthetic process [74] (Andreiadis et al., 2011). In this strategy a photosensitizer molecule to power the system (P; figure 10), is linked to a water oxidation catalyst and a hydrogen evolving catalyst. This mimics the first step of photosynthesis, when a light-harvesting complex captures photons and transduces them into electrons. The electrons are next transferred to hydrogen catalyst (A; figure 10). When the photosensitizer is hit by light it undergoes oxidation and this drives the water splitting catalyst to donate electrons to the photosensitizer, hence referred to as a donor (D; figure 10). The oxidized donor is able to oxidize (split) water to $H^+$ (utilized for dihydrogen production) and $O_2$ [74] (Andreiadis et al., 2011).

There are many possibilities as to how to create an ideal triad assembly that could efficiently perform artificial photosynthesis [75]–[77] (Hammarström & Styring, 2008; Kalyanasundaram & Graetzel, 2010; Megiatto Jr et al., 2014). One example involves the utilization of a silica material that can serve as a platform to assemble and couple photocatalytic components for the direct conversion of water and $CO_2$. In this case two functional units were used, a light-absorbing electron pump (Cr centre) coupled to a multielectron-transfer catalyst for water oxidation (Ir oxide nanocluster). The trials demonstrated that no $O_2$ was formed in the dark and that water oxidation is driven by the charge-transfer-excited Cr complex coupled to Ir oxide cluster. This suggests that covalently anchored metal centres could be used as charge-transfer chromophores for coupling the oxygen-evolving site to a reducing metal-to-metal charge-transfer unit in the nanoporous solid [78] (Nakamura & Frei, 2006). Alternatively, one could use a liposomal membrane with artificial triad coupled to the natural ATP- synthase [79] (Steinberg-Yfrach et al., 1998). This approach indicates yet another possibility of bio-synergy - that is assimilating technology and biology.

Multiple approaches can contribute to solar fuels future. None of them prove to be a definite answer and all of them are still on the basic research side. Using an interface to the USPTO to map 78 available patent portfolios related to artificial photosynthesis [7] (Leydesdorff, Kushnir, & Rafols, 2012), we have noticed that no definite "cluster" appeared. This further illustrates that multiple lines of research exists and shows that the comprehension of translation process is growing and will sooner or later yield commercial results. The key areas that can contribute to the ultimate solutions are: architectures (for controlling of electron transfer), catalysis (catalysts for water oxidation, or $CO_2$ splitting), devices (e.g. improving the efficiency of water splitting), photocatalysis, mechanisms and theory. The overview of progress in mentioned areas can be found in [80] (Concepcion, House, Papanikolas, & Meyer, 2012).

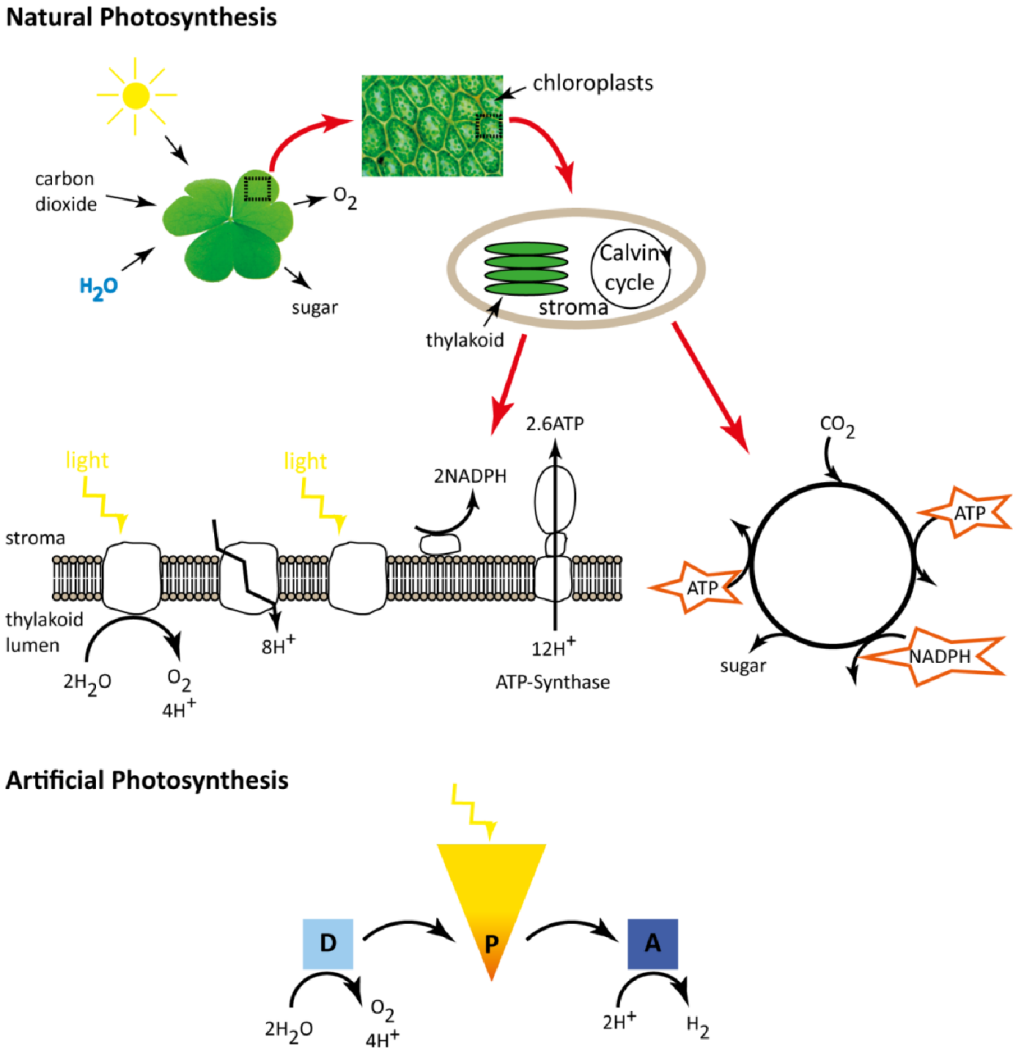


***Figure 10. Natural vs artificial photosynthesis***

The above section 6 related to future energy source has been subject to semantic analysis performed by two different search engines then clustering. The study was performed on the first 1000 most relevant patent references for the sake of processing ease. Obviously the two searches converge as per comparison of the left and the right gearwheels clusters on figure 11.

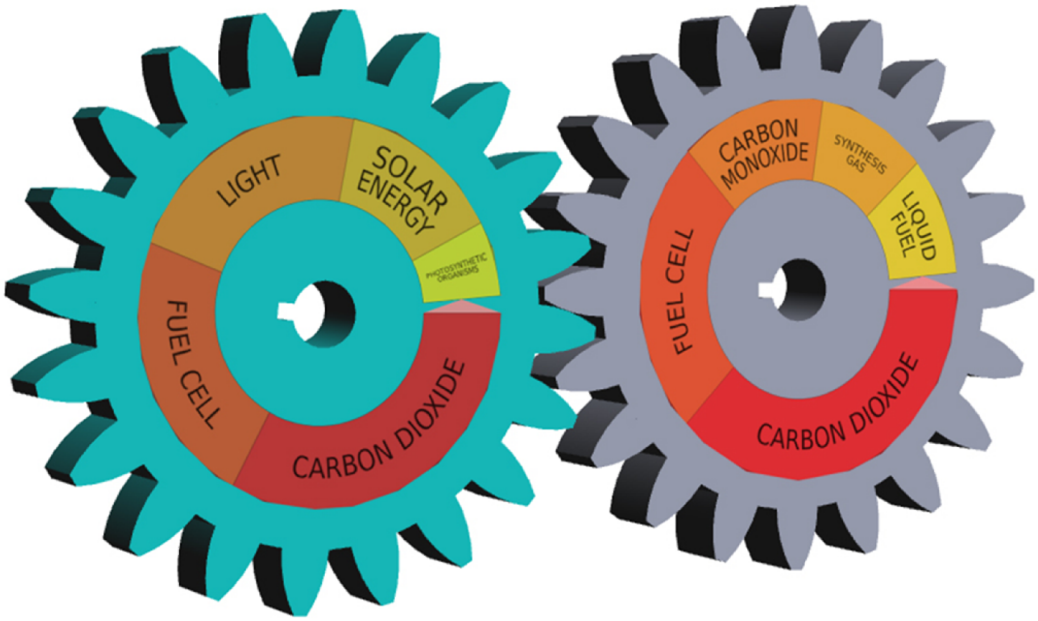


***Figure 11. Semantic analysis and clustering of section 6 – "Future Energy Source"***

## 7 HOW TO TACKLE THE PERFECT DESIGN AND PRODUCTION OF NATURAL POLYMERS?

The observation of nature boosted the increase amount of innovative materials that come to life such as previously mentioned Velcro, honeycomb-like structures or SLIPS [47] (Aizenberg et al., 2012), to name a few. In the case of material innovation, the mimicry approach is not always as straightforward and easy as imitating lotus leafs surface because strategies for design differs between engineers and nature. The biggest obstacle is to transfer concepts and procedures used in natural settings, simply because we yet lack insight into those processes. These are however, the core causes that decide about properties of materials. Development of material is constructed in an opposite way, engineers first choose the material and then create it (top-down approach), and nature would start with material at hand that will self-assemble (bottom-up approach). The resulting hierarchical structure of natural structures gives certain advantages that we desire to imitate, including resistance, multifunctional or adaptive properties and self-healing capacity. A simple and imaginative example is a design of material modelled on shark skin. The surface of the shark's skin is very rough, under closer inspection it turns out to have little structures, described as V shaped or tooth like, and called dermal denticles [81][7]. They are aligned parallel to the flow of water; producing vertical spirals of water that ultimately reduce surface drag. Engineers were inspired by the microtopography of shark's skin that, in the same time, acts as an anti-fouling and anti-bacterial material that does not necessitate the addition of toxic agents [82] (Carman et al., 2006). A material with this set of properties can be used on any surface that needs to be kept clean such as medical devices [83][8].

Materials that belong to a group of polymers are everywhere in our surroundings. They can have either natural origin (such as DNA, wool, silk or cellulose) or be synthetic ones (including nylon, polyvinyl chloride, silicone, and many more). Polymers, in their simplest form, are chains of bonded small molecules (monomers) with multiple applications. One method to produce them is a process known as radical polymerisation. It uses very reactive molecules with unpaired electrons (free radicals) that initiate a chain growth by adding to monomer unit. In turn, it will generate a new radical and repeat the process. However, this process often yields various structures, molecular weights, and lengths of polymers. To gain more control on the procedure of polymerisation scientists were inspired by the natural approach of polymer synthesis. Organisms are using templating synthesis, such as transcription of nuclear DNA into messenger RNA, followed by peptides creation. In

[7] *ocean.si.edu/ocean-photos/biomimicry-shark-denticles*
[8] *sharklet.com*

addition, to ovoid the undesirable interactions between elements, reactions are carried out in separate cell compartments. Scientists specifically mimic a combination of segregation and templating seen in cells to gain precise control over the organisation of polymers during radical polymerisation [84] (McHale, Patterson, Zetterlund, & Reilly, 2012). This is a great example to illustrate an earlier point that inspiration provided by nature can be purely on conceptual level and doesn't mean we have to use bio-materials to achieve it. The next paragraphs further illustrate this point.

Silk is an exceptional natural polymer with a unique set of mechanical properties and efforts have been made to produce a material with similar characteristics. The idea being to copy spiders and insects several types of silk designed to achieve a range of functions from prey capturing and immobilization to reproduction. Technically, silk types consist of repetitive blocks of crystalline domains (beta sheets; made mainly by two types of alanine rich regions) and so-called amorphous matrix (consisting of helical and beta turn structures glycine) with the addition of various compounds other than protein that enhance the fibre's properties [85] (Simmons et al., 2014). Nature's high - performance fibre exhibits a unique combination of high tensile strength and extensibility so that the energy required to break spider silk (toughness) can be 10 times greater than for any other biological materials (cellulose, collagen, chitin).

***Spider vs other macromolecular materials: Strength ($N/m^2$)-mid vs Energy to Break (J/kg)-right [86] (Lewis, 1992)***

| | | |
|---|---|---|
| Dragline silk | $1 \times 10^9$ | $1 \times 10^5$ |
| Kevlar® | $4 \times 10^9$ | $3 \times 10^4$ |
| Rubber | $1 \times 10^6$ | $8 \times 10^4$ |
| Tendon | $1 \times 10^9$ | $5 \times 10^3$ |

A commonly proposed structural model for the silk fiber, "with highly oriented alanine-rich crystals, and with weakly oriented "protocrystals" contributing to the unusually high compressive strength of spider silk", is generally proposed after Jelinski and co-workers. In this model, "glutamine and other bulky residues limit the growth of 3 sheets and force the formation of loops and tie chains that link crystals to one another and to the surrounding amorphous matrix. This picture is consistent with a theoretical model of spider silk elasticity developed recently by Termonia at DuPont [87] (Termonia, 1994), in which the fiber is represented by small crystallites embedded in a rubbery amorphous phase. A key feature of the Termonia model, which reproduces the stress-strain behavior of the fiber very nicely, is the presence of a thin layer within the amorphous matrix with a modulus higher than that of the bulk amorphous phase. Small crystallite size is advantageous in this description, as it allows the high-modulus "interphase" to occupy a large volume fraction in the semicrystalline fiber".

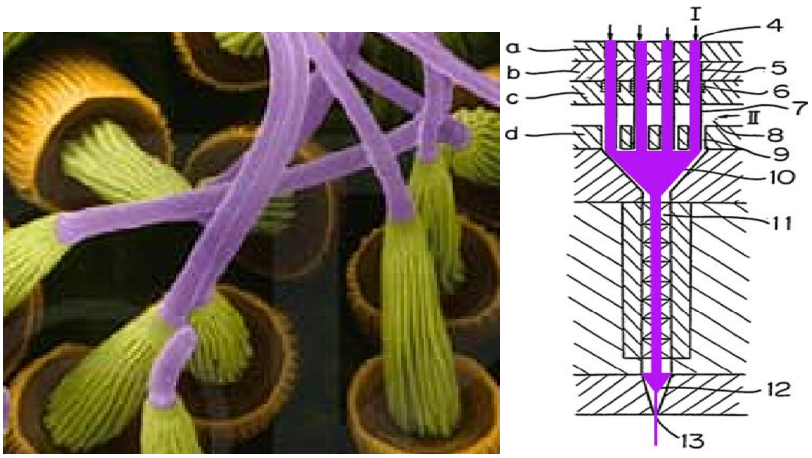


***Figure 12. A spider spinneret with silk spinning spigots. Copyright & Credit [88] (Dennis Kunkel Microscopy, Inc.) And a spinneret assembly analogue (right) from [89] (Hiroyasu et al., 1983)***

Spiders' silk is a protein rubber, it means that at room temperature it is stiff; however upon immersion in water it will absorb it and contract to half of its length. It is the interplay between the hard crystalline segments, and the strained elastic semi-amorphous regions that gives spider silk its extraordinary properties [90] (Gasline, Denny, & DeMont, 1984). To mimic and perfect the process of natural silk production we need to combine both the feedstock proteins from which the silk is produced, its post-translational changes along with the spinning process itself [91] (Vollrath & Knight, 2001).

Back in 1996, in the Science News, Vol. 149 No. 10 p. 152, one could read the following:

"- "Cloning the entire silk protein is not necessary, agrees John P. O'Brien, a chemist at DuPont Co. in Wilmington, Del. "We think we can mimic most of natural silk's properties with much simpler polymers and produce them large-scale."

"Silk has a lot in common with reinforced rubber," he adds. "This allows us to use theories of rubber elasticity to design the synthetic fiber's architecture."

To reduce the length and complexity of the synthetic protein, DuPont Life Sciences chemist Stephen R. Fahnestock says his group has homed in on four short amino acid sequences from one of the two major proteins. By implanting a synthetic gene for those sequences, his team has coaxed bacteria and yeast into producing a novel protein, which DuPont is spinning like conventional polymers into fibers.

"They're not quite like natural spider silk," says O'Brien, "But they're still good when woven into multifilament yarns."

Kenn H. Gardner, a biophysicist at DuPont, points out that spider silk, both the natural and new synthetic versions, is essentially a form of nylon. "That's our business," he says.

"What's particularly interesting to us is the way these organisms make silk nylons in environmentally benign ways," O'Brien says. "They process proteins from water-based solutions, without using petroleum products or organic solvents. From a manufacturing point of view, this is very attractive."

Given the "consumer love affair with natural fibres," he adds, "we want to offer substitutes for natural fibres that are free of associated problems, such as poor wash-wear performance, stretching, wrinkling, and shrinkage."

"Ideally, we're aiming for a better-than-natural alternative fibre." -"

Obviously, with Termonia's predictive models, the spinneret (bio and mechanically illustrated on figure 12) advanced core technology of the company employing him, and thanks to the O'Brien's multidisciplinary team, the science and technology enterprise was in good hands. Bio-inspired materials were paving new frontiers for the fibre technology and business therewith.

This brings us to goats. Silk-producing goats were firstly bio-engineered and held by a Canadian company. A lot of hopeful press coverage in the mid-2000s for the BioSteel®, a spider silk-based material. By 2009, though, the goats had all but vanished from headlines news.

There is likely a lot to learn about open innovation and disruptive innovation with this case. Shall the bio-inspiration be limited to curiosity provocation and confidence gaining, at first; therefore yielding creative multiple concepts? Or shall one let engineering take over "immediately" based on core technology comforting knowledge therewith avoiding lateral thinking exposing uncertainty?

Up to date, inspiration of silk may have contributed to producing of synthetic fibres branded as Kevlar® (developed by DuPont in 1965; [92][9]) and later on as Twaron® (developed by ENKA in 1972; [93][10]). Currently, the USPTO registers 13,452 patents that contain the word ''Kevlar'' (Feb, 2014) that points out to its spectacular success and wide range of applications. It is used in protection clothing for military or personal use (helmets, vests, masks, and gloves), sport (tennis racquet, sport shoes) or music equipment (loudspeaker cones), can be used to make ropes or as a protective outer sheath for optical fibre cable, and many more [92][11]. Rebouillat et al., published abundantly in the field [94]–[100] (S. Rebouillat, Donnet, & Wang, 1997; S. Rebouillat, Liksonov, & Courgey, 2012; S. Rebouillat, Steffenino, & Miret-Casas, 2010; S. et al. Rebouillat, 1998; S. Rebouillat & Liksonov, 2010; S. Rebouillat, 1998, 2001).

[9] *www.dupont.com/products-and-services/fabrics-fibersnonwovens/fibers/brands/kevlar.html*

[10] *www.teijinaramid.com/aramids/twaron/*

[11] *www.dupont.com/products-and-services/fabrics-fibers-nonwovens/fibers/brands/kevlar.html*

The next example of a natural polymer that we try to mimic is muscles. In essence, there are multiple chains of muscle fibrils (or myofibril), that in turn are long proteins strings (composed of actin, myosin, titin, and others) [87][12]. Artificial muscles are needed to develop prosthetic limbs, robots or actuators. Recently, inexpensive and high-strength polymers, specifically polyethylene (PE) and nylon fibers [101][13], were explored to be muscle precursors [102] (Haines et al., 2014). Due to their flexibility they can be reversibly contracted, twisted and therefore mimic the function of torsional muscles. Interestingly, it is possible to convert the twisted fibers to complete coil and this allows to exceed the maximum tensile contraction by 20% compared to human skeleton [102] (Haines et al., 2014). To create larger diameter coils, one can wrap twisted fibers around mandrel and stabilize the shape with heat. The resulted coils have reduced load capacity but can contract more, hence has larger stroke [102] (Haines et al., 2014). A coiled nylon muscle, powered by applying potential, successfully delivered 1.2 million cycles of rising and lowering 10 g weight without any significant creep. In addition, fast and high force actuation can be driven hydrothermally, authors driven coiled nylon muscle by switching between cold and hot water up to 1500 cycles under a 0.5 kg load. In a similar manner PE fiber muscle, with the addition of surfactant to enable wetting of the material, could lift 7.2 kg load generating mechanical work output 100 times more than the human biceps muscle. Series of experiments showed that a specific mechanical property of proposed artificial muscles depends on their structure and scale and suggested a variety of applications [102] (Haines et al., 2014).

The above section 7 related to natural polymers has been subject to semantic analysis performed by two different search engines then clustering. The study was performed on the first 1000 most relevant patent references for the sake of processing ease. Obviously the two searches distant themselves substantially as per comparison of the left and the right waterwheels clusters on figure 13.

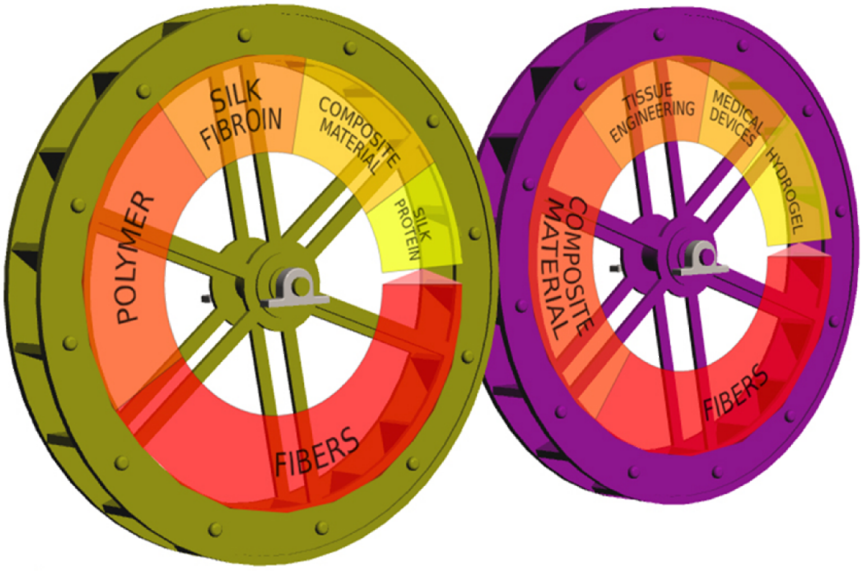


***Figure 13. Semantic analysis and clustering of section 7 – "Natural Polymers"***

## 8 FINAL REMARKS

Open disruptive innovation is probably an inevitable challenge to maintain the pace of changes occurring in some technology areas. Creative confidence is to be reinstated in the broader creativity scheme which embraces a much larger range of functions than the ones generally anticipated.

[12] *muscle.ucsd.edu/musintro/jump.shtml*
[13] *plastics.dupont.com/plastics/pdflit/europe/zytel*

Bio-inspired or bio-inspiration is a well of analogues that can translate into discovery beyond the logic of invention as traditionally conceptualised.

In everyday life "Semantic" has already evolved towards the integration of images and motion, as part of everyday communication and interpretation of events. Innovation is concomitant to that evolution. Patent search engines remain mostly centred within the logic of patent classification and search algorithms which may not be the most powerful stimulus for innovation, open innovation and disruptive innovation.

ATA©, adjacent technology analysis, tends to reduce this gap and is subject to other papers of the authors [1], [2] (S. Rebouillat & Lapray, 2014; S. Rebouillat, 2013).

Rebouillat et Lapray (2014) [2], devoted a full review to patent search aspects. In the present study the use of semantic to collect patent literature from the same text excerpt reveals large to moderate variations in the resulting outputs in term of clusters. Black boxes around patent searches may have to be more explicitly unveiled to avoid user confidence depreciation.

There are endless list of examples of bio-inspired technologies in every area of modern technology [103][14]. Only few of them have been noted in this review. We believe that there is many more to come. Why not to exploit the cryotolerance mechanism of the leech (turtle parasite) capable of surviving exposure to -90°C for up to 32 months [104] (Suzuki, Miyamoto, Kikawada, Watanabe, & Suzuki, 2014) or re-invent a way to fly by looking at the gliding technique of snakes favouring the "S" posture for that purpose [105] (Socha, 2002)? Reader can be further inspired by below reference list.

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[14] *www.asknature.org*

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