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New techniques for the alteration of the living

For whom ?

Why ?

POUR L'EMERGENCE D'UNE
Université du Vivant

This brochure is mainly inspired from the workshop “The coming modified plants, why et for whom ?”, an Inf'OGM's training on the new techniques of biotechnology, october 2010, the 5th and 6th, Bagnolet (93) France.

This brochure is by :

Inf’OGM - http://www.infogm.org/
Inf'OGM is a citizen watchdog, following worldwide news on genetically modified organisms and biotechnologies. Inf'OGM produces and spreads independant and critical information so everyone can make its own decision. It aims at obtaining a true transparency from public authority.

With the collaboration of :

BEDE - www.bede-asso.org
BEDE is an international association founded in 1994. It is based in Montpellier and has been set up as a French non-profit organisation.
Together with close to fifty organisations that belong to French, European and international networks, BEDE is contributing to the protection and advancement of family farming by supporting information dissemination and networking initiatives managed with due respect for living organisms diversity. BEDE produces teaching tools and organises workshops, meetings for farmers, researchers and representatives of the civil society from around Europe, and from North and West Africa. Through its activities BEDE enables the public at large to understand what is at stake with agricultural biodiversity and helps farmers organisations to improve their work in the field and their capacity for legal negotiations on genetic resources, biosafety, intellectual property rights.

GIET - http://giet-info.org/
The International group of interdisciplinary studies (GIET) is a cultural association created in 1996. It aims at thinking the nature of science and promote interdisciplinarity. This group, mainly constituted of researchers, is actually based in Belgium, Germany, United-States of America and France.

RSP - http://www.semencespaysannes.org/
In France, the Réseau Semences Paysannes (farmers' seed network) was founded in 2003 in response of the lack of suitable seeds for smallholder, organic and biodynamic farming and also the refusal of the use of biotechnology in the plant breeding, which was becoming widespread. It now gathers 60 member organisations across France including several farmers'organisations and organic farming organisations, artisan seed producers and nurseries, farmers, gardeners, development NGO and organisations of biodiversity conservation. They are national, regional or local organizations.
As a network, its mandate is to link initiatives related to the conservation and renewal of cultivated biodiversity, facilitating this network of knowledge and know-how through information dissemination and capacity building of its members, through exchanges and training. The RSP also plays a leading role in developing partnerships with the scientific community in the public sector through participatory and innovative research projects.

The present report, published in september 2012, was first published in french in october 2011.

Plant genetic engineering with laboratories' technique is a process still going on in the biotech companies' laboratories. The current commercialised GMOs come from technique already obsolete. For transgenesis is no longer the only technique adopted by the industries to genetically modify plants. The technicians have now the choice between several technique with names such as zinc finger nuclease technology, cisgenesis...

Focusing on the risks associated with transgenesis, which allows the genetic chimera development, public debate got recently interested in older genetic engineering technique like mutagenesis. This debate on mutated plants did not occur prior to their commercialisation which happened with no legal biosafety framework. New techniques that are now coming out from laboratories require public attention.

By the end of 2008, European commission requested from membre states two experts to join a european working group. Its goal was to answer the following question : does GMO legislation applies to products obtained through the use of those eight techniques ? In june 2011, the experts had not finished their work and no calendar was known by then.

To answer this new move of technoscience, a seminar was organised by Inf'OGM in order to start thinking an independent and critical analysis. With the purpose of having a democratic debate with sufficient knowledge.

Preface

Frédéric Jacquemart, President of Inf'OGM

Techniques for the genetic alteration for living organisms[1] are undergoing very rapid change. Where do the products of new technologies stand in terms of European directives and regulations? This is a question currently under consideration, and the European Commission (EC) has formed a committee of experts (with two experts per Member State) to help provide an answer. The legal status of these products will depend on decisions made by this committee.

One concept that is clearly of interest here is the legal definition of a genetically-modified organism. According to European law (Directives 90/220 and 2001/18)[2], a GMO is "an organism, with the exception of human beings, in which the genetic material has been altered in a way that does not occur naturally by mating and/or natural recombination". Having said this, exceptions do exist and are listed in the same directive. Thus, under article 2.2b, in-vitro fertilisation, natural processes (conjugation, transduction, transformation) and polyploid induction* "are not considered to result in genetic modification". Above all, however, there are two techniques that, while recognised as producing GMOs, are excluded from the scope of the directive under article 3.1. Thus, "this directive shall not apply to organisms obtained though the techniques of mutagenesis* and cell fusion*". This existing exception is based on the work the European Commission requested from the group of experts that has met since 2009, and which is supposed to establish "a list of techniques that come under the scope of Directive 2001/18 on the deliberate release into the environment of genetically-modified organisms and Directive 90/219 on the contained use of genetically-modified microorganisms"[3].*

In short, and to be clear, European law draws a distinction between two types of GMO: those included within the regulatory framework for biosecurity, and those that are not. As a result of this exclusion, the latter are illicit. Yet these illicit GMOs are readily available on the market without any evaluation of their effects on human health and the environment, and do not meet the labelling requirements demanded by citizens for conventional GMOs. These are living organisms created using non-natural methods and which can cross-breed with other organisms when released into the environment. Moreover, these GMOs that are the product of genetic modifications can also be patented, and therefore play a part in the private appropriation of whole fields of living organisms.

At the time this brochure went to press, the European committee of experts had not yet delivered the final version of its report to the European Commission, two years after it was formed. While amendments are currently being made to European law and may be reviewed in 2012, this report should have been made public earlier in order to allow fair public debate with civil society and business representatives, and allowed sufficient time to prepare an in-depth analysis of the socio-economic and cultural issues connected to the proposed technologies.

Given the evolution of techniques used to alter living organisms by genetic modification, the status of the organisms produced by these processes must now be clarified. Are these organisms GMOs? And, if so, should they be included or excluded from the scope of the directive? Thus, does site-directed mutagenesis with the use of oligonucleotides that disappear after several cell divisions fall within the scope of this directive? Can transmissible epigenetic modifications* be considered genetic "modifications" (this term is too vague here) ?*
And so on.
We can clearly see the consequences of the answers to these questions for seed companies on the one hand and, on the other, for citizens: depending on decisions made, a product would have to be evaluated, traced, possibly labelled, etc; otherwise, it could be considered a perfectly normal organism with no restriction on its commercialisation, and totally unidentified. This is a considerable issue for experts, in particular in view of the desire of the European Commission to push biotechnology-based agricultural products through at all costs, in support of the interests of the highly competitive industrial sector to gain global control of the food chain. The industrial property rights that ensure this control are evolving with technology. The European seed industry, whose prosperity is based on the New Plant Variety Certificate (NPVC), is gradually being taken over by multinational firms of the chemical sector that are investing heavily in patented biotechnologies. Competition between different forms of intellectual property law (NPVC and patent) fail to hide the existence of the industry's sole plan: that of appropriating living organisms by increasing their market share. How will new technologies of genetic modification help meet this objective this objective?

Non-traceable techniques have the advantage of easily avoiding the order to provide compulsory information that could lead to consumer rejection. However, their disadvantage is they cannot provide irrefutable identification of intellectual property.

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[1] Complex plants and animals, bacteria, fungi... all living creatures are currently the object of genetic modifications.

[2] Directive 90/220: http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX:31990L0220:FR:HTML
Directive 2001/18: http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX:32001L0018:FR:NOT

[3] Terms of reference for the « working group on the establishment of a list of techniques falling under the scope of directive 2001/18/ec on the deliberate release of genetically modified organisms into the environment and directive 90/219/eec on the contained use of genetically modified micro-organisms », Bruxelles, ENV B3/AA/ D(2008)

To enable readers to also follow current events and be up-to-date on the latest developments in genetic technology (and agricultural applications), Inf'OGM aims to provide insight into the new techniques now being evaluated by experts to as broad a public as possible. However, since the details are of little importance to the uninitiated, summaries of these techniques will be provided.[4] What matters most is being able to understand how they are part of a public debate.
The other aspect that justifies the inclusion of this document in the PEUV association programmes relates more to the analysis of the meaning of this frenetic modification of living organisms, which gives the impression that everything that can be done should be done, and the sooner the better.

A symposium on the same theme of new technologies, organised by the HCB[5], was held after that organised by Inf'OGM and PEUV for activist of this sector; this document is the culmination of these efforts. These seminars enabled researchers, who themselves often promote these techniques, to explain them to members of the HCB. In addition to this compulsive appropriation of all genetic and epigenetic material that can be used to control living organisms, which is considered a mere tool in the purest of Baconian traditions,[6] what was striking was the constant emphasis given to a response to technical criticisms (or evasion thereof) levelled by those opposed to GMOs: that the organisms produced by the use of these techniques "are not GMOs" and have properties that made modifications impossible to detect (no one will ever know about them).

It is clear to us that technology can provide a answers to technical objections made to other technologies. But this is mere dissimulation: the said technology is masking the basic issue that is none other than modernity itself, that of a world hurtling ahead at full speed without any sense of direction, of a dominant culture that is destroying its own living conditions. This is what has motivated t the descriptions of techniques that are useful in practice but anecdotal in substance, a reminder of changes in industrial property rights on plants, and what explains who benefits from the modifications made, and a more general analysis of the reasons why GMOs exist, and the artificialisation of living organisms.

** The terms followed by an asterisk are defined in the glossary at the end of this work.*

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[4] For more information, more detailed descriptions can be found on the Inf'OGM website (http://www.infogm.org).
[5] High Council on Biotechnologies. This official council aims at providing the french government with opinions on biotech files, notably those concerning the intended release of GMOs in the environment.
[6] In the 17th century, Sir Francis Bacon used to consider that the science's goal was to fight against and defeat nature. Contemporary science still takes its roots in Bacon's, Descartes' and Hobbes' ideas.

Contents

Introduction

GMOs have been part of a broad public debate since their introduction into agriculture on a massive scale in the mid-1990s. As of 2010, GMOs were grown on an estimated 148 million hectares of land. Of this land, three-quarters was in the Americas.

A market controlled by multinationals of the chemicals sector

The continuous expansion of crops of genetically-modified plants (GMP) is a response to specific industrial interests, the expansion of the chemicals sector (Monsanto, Syngenta, Dupont, Dow Chemical, Bayer, BASF). This sector invests billion of euros in biotechnology every year, and the growth of the seed sector based on a tradition of plant breeding, particularly in the production of varieties that cannot be reproduced by farmers, such as F1 hybrids, the only maize and sunflower seeds sold in France. These two sectors are both rivals and allies: in recent years there have been numerous mergers (see note 25), with the result that almost 80% of the commercial seed market protected by industrial property rights is now controlled by chemicals multinationals.

The chemicals sector effectively provides an increasing proportion of agricultural inputs: fertilisers, weed-killers, phytosanitary treatments, and many additives to stimulate yield and provide post-harvest protection. With genetic modification of plants, varieties can be tailored to their product. The most illustrative example is that of Monsanto, a company that has developed hundreds of Round-up ready varieties, resistant to their own weed-killer, Round-up. This is true for two thirds of GMP crops over the last fifteen years.

What is much more attractive for investors in plant biotechnology, however, is the ability to create monopolies in the agrifood sector thanks to patents on technologies, genes and organisms. Gaining control of the first link in the food chain (seeds) is the object of internecine strife between the forms of industrial property rights, which we will discuss in greater detail in chapter two. While competition for the largest share of the seed market within the industry is fierce, an even larger share of plant genetic resources are being privatised and a growing number of farmers are being deprived of their rights to breed, save, multiply, exchange and sell the seeds they grow.

An observation of the development of the plant biotechnology sector clearly reveals the need for ongoing technological innovation that justifies the existence of industrial property rights for actors in this sector. The number of patent applications for genes and their functions is rising sharply. Techniques that could significantly alter the functioning of cellular metabolism and in particular of DNA, the molecule that carries hereditary information, are the focus of intense research and development. Transgenesis, which was considered a revolutionary technique to genetically modify plants 25 years ago, has now been overtaken by other more recent findings. New nanotechnologies that transform living organisms are rapidly increasing, and the first applications of synthetic genomes to bacteria indicate that transposition to plants will soon be be possible.

While the chaos unleashed by the first GMOs is far from over and still mobilises a broad coalition of farmers, researchers, consumers, environmental and civil society organisations, manufacturers are actively preparing new generations of modified, higher-yielding living organisms which they hope will have none of the negative effects of their predecessors.

Reasons for, and results of popular opposition

Returning to opposition to first-generation GMOs (those currently on the market), it is useful to recall the main reasons why they were rejected by civil society, and the results achieved by the opposition movement.

Given that this issue has been explored in a number of works (read in particular "OGM: La bataille de l'information"[7]), we will address four main objections in summary form.

The first objection relates to genetic engineering technologies themselves. Tinkering with DNA influences the nature of species, the relationship between species in an ecosystem (whether natural or cultivated), and future generations. Indeed, these intrusive modifications affect the main molecular support for heredity, while the irreversibility of the release of artificial genes raises deep concerns. It is difficult to imagine that the equilibria of living systems will not be affected by the results in particular of transgenesis, a process that involves mixing the genes of organisms as different as goats and spiders, fish and strawberries. Can the joint evolution of species (including humans) come out of this unscathed?

The second objection raises the more specific threats posed by the impacts of transgenic plants on the environment of agricultural systems, and on consumers' health. These aspects have been extensively studied for almost two decades, and are still the focus of divergent interpretations. Results have progressively confirmed that the decision to put GM plants on the market was a disastrous one: rural regions in Latin America completely devastated by GM soy monoculture, the inability of GM plants to coexist with other forms of agriculture and, significantly, with organic modes of production (the disappearance of organic rapeseed in Canada and organic maize in Spain), a red warning light on biodiversity indicators in all GMP production areas, the increased use of herbicides that have had direct impacts on the

[7] Inf'OGM, OGM: La bataille de l'information Des veilles citoyennes pour des choix technologiques éclairés, edited by Charles Léopold Meyer, 2011, 308 p. http://www.eclm.fr/bdf/ouvrage-347.html

health of people living in rural areas, a wave of suicides among farmers who have fallen into debt as a result of GM cotton in India, etc. In terms of the safety of foods from genetically modified plants, there are no credible epidemiological studies that can confirm the absence of health impacts on various target groups. However, several toxicology studies have confirmed the harmful effects of certain GMOs tested on the development of internal organs and deficiencies in blood tests in lab rats. The European Commission is still unable to provide a response to the issue of the toxicity of Mon810 maize. Furthermore, chimeric gene constructs containing ARM genes have been banned for public health reasons after a long debate between experts.

The third complaint arises from new forms of intellectual property authorised on plants whose genes have been modified using technological means, with industrial patents now integrated into the genetic inheritance of living organisms. The right of farmers to resow commercial varieties of plants from seeds they had saved had already been undermined to a considerable extent by industrial seed companies, who claimed plant variety rights to patented varieties. With the gene patents and their functions, transgenetics can be used to monitor intellectual property in farmers' fields. The prosecution of hundreds of farmers in North America by large companies such as Monsanto and the decision handed down by the Supreme Court of Canada in favour of Monsanto in view of the farmers users' rights (Monsanto v. Percy Schmeiser) emphasises the contentious nature of relationships within the industrial farming sector, and justifies the determined mobilisation of farmers' organisations in their rejection of patented GMPs.[8]

The fourth main objection is the lack of democracy in technological choices made. The first issues in this regard became apparent very early on, in the form of difficulties accessing verified information and contradictory studies by experts. Public sources on the evaluation of risks were not much more explicit. A lack of resources and clauses to protect the confidentiality of research projects were frequently cited as excuses for the absence of data. Subsequent official expertise was found to be dubious, ambiguous and a source of debate between groups of experts. Clear conflicts of interest were exposed between decision-makers and manufacturers, with experts becoming adept at the playing the system of revolving doors between agencies providing expertise, ministerial staff, and works councils. Given the difficulties in establishing an open public debate and the bias of the authorities responsible for establishing this debate, civil society mobilisation has come to the fore, creating mechanisms for debate (trials, fora, citizens' juries) to query the basis of guidelines for research on GMPs.

Society's concerns about how appropriate it is or is not grow transgenic plants were widely expressed in the ten years between 1998 and 2008. These struggles have produced significant results that strengthen regulatory frameworks for evaluation and marketing conditions for these plants. Between 1999 and 2004, European directives on biosecurity were completely reviewed, and regulations on the traceability and systematic labelling of products containing GMOs put in place. NGOs and farmers' organisations developed expertise, collaborating with researchers and whistleblowers and conducted independent studies on risk evaluation that produced a number of results on both technical and legal issues. Civic information watchdogs were set up with a number of intermediaries in the regions, covering the territory with with civil society flagging tests. From an institutional perspective, in France in 2008 opponents of GMOs secured the transposition of the European directive of 2001, a moratorium on the only GMP authorised for cultivation, Mon810 maize by Monsanto, and more active participation of civil society in a consultative body (the High Council for Biotechnologies).

[8] Noisette C., "Etats-Unis - Une nouvelle plainte contre les brevets et les OGM de Monsanto considérés comme 'sans utilité sociale'. Inf'OGM, June 2011.

1. Principles and applications of new techniques for the modification of living organisms

The current regulatory framework for biosecurity on GMPs concentrates essentially on a single technology, transgenesis. Transgenesis produces a transformation of living organism that is so radical that legislators have found it necessary to provide a legislative framework; it is the red line that has put a stop to the unregulated application of biotechnological research on plants. Thus, since 1990 varieties grown in Europe produced by transgenesis have been subject to particular treatment in relation to the evaluation of risks and their release into the environment. Given that transgenesis is used as a reference for experts when setting limits to the transformation of living organisms, which must be subject to the strict application of the law, we will start with a reminder of its characteristics.

We will then present seven of the eight new techniques now assessed by the European Commission. The eighth technique (synthetic biology), which is a product of an even more radical advance in the artificialisation of living organisms, will be addressed separately in Part Three.

All of the techniques for the modification of living organisms presented here in a very simplified manner are in fact series of highly complex processes subject to rigorous protocols that involve a number of technical and conceptual tools in molecular biology. They are difficult to understand even for scientists, and even more difficult to evaluate. At this very high level of specialisation, there are even fewer independent experts given that most funding comes from the private sector and is subject to confidentiality clauses. Therefore, the civic society watchdog on GMOs has decided to decipher what these new manipulations entail, and to understand how plants produced by these modifications compare with current GMPs. With the cooperation of public research scientists, it has been possible to understand the main principles that drive these new developments, so as to provide the public with information that is essential to analysis.

Brief overview of the evolution of concepts and techniques in genetics

While the earliest notions of the transmission of characteristics from one generation to the next were formulated by Gregor Mendel in the 19th century, it was not until the 20th century that it was shown that DNA was a factor in the transmission of characteristics and that this molecule had a double helix configuration, within which the base elements (nucleotides* adenine (A), thymine (T), guanine (G) and cytosine (C)) match, like matching steps on a ladder, A with T, and C with G.[9] DNA is present in all cells and assists in the their multiplication, producing identical replicas. While replicating itself, the DNA molecule is open and each piece of the double helix is exposed to proteins that are able to replicate it. During the cell division the two DNA molecules then split into new nuclei in the process of formation. This phenomenon is the basis of all current work on genetics and biotechnology.

With cycles of cell division, the DNA molecules that comprise the genome (all genes in an organism) can become compressed to form chromatin, which itself will be structured as chromosomes. The notion of the gene remains a theoretical construct that is difficult to establish. But in simple terms, a gene could be described as a specific DNA sequence that, when read, will result in protein synthesis.

Information stored in DNA within the nucleus cannot be extracted without RNA*, which can copy a DNA sequence (this is referred to as the "transcription" of DNA onto RNA) and carry this information outside the nucleus, to the cytoplasm of the cell. There, this information allows certain elements of a set of amino acids to organise themselves into a specific protein (this is referred to as the "conversion" of RNA into protein).

Thanks to technical progress in DNA sequencing methods that consist of identifying the sequence of nucleotides, we can now determine any DNA sequence and, using new polymerisation techniques* (PCR), reproduce it in a few hours for a few hundred euros. This knowledge of the nature of DNA itself, its double helix formation and, above all, the matches between nucleotides, the genetic code, gene sequences, PCR, and sequencing techniques, has opened up the path to the genetic technologies that are now being developed.

While these discoveries have provided ever more accurate explanations of the nature of information passed on from one generation to another through living systems, other discoveries have led to a re-emergence of notions that are just as important but which have to some extent been neglected, as a result of the focus on DNA research. Thus, work in the area of epigenetics (the study of modifications that can be passed on via hereditary means with no alteration to the DNA sequence) shows that the characteristics of an organism can be passed on through elements other than the gene sequence alone. To a large extent, the "one gene = one protein = one characteristic" dogma has been widely contradicted.

It should also be remembered that almost all new techniques described here, have the objective of breeding new varieties of cultivated plants, and are therefore incorporated into programmes where cells rather than the entire plant are selected. Once the DNA of the cell has been modified, the cell is placed in a culture environment containing growth hormones to generate a plant. Nevertheless, in-vitro culture technologies, which have existed for some 50 years and to a large extent been developed for almost all species, are not neutral vis-à-vis natural equilibria and must be questioned, as we do in the conclusion.

Transgenesis: The reference technique

Drawing on scientific knowledge of the mechanisms of genetic heredity, transgenesis is the product of techniques developed and discoveries made in the 1970s that enabled the modification of DNA and were grouped together under

[9] "Molecular Structure of Nucleic Acids: A Structure for Deoxyribose Nucleic Acid", Nature, no.171, April 25, 1953, pp. 737-738.

the term "genetic engineering". The principle is to transfer a gene from any species to any other, eliminating the need for sexual reproduction and other biological barriers. A DNA sequence from an animal or a human being can, in this way, be transferred to a cultivated plant and express a new characteristic for the species; the gene can then be passed on hereditarily from one generation to the next. In the main GMPs commercially available (Bt maize, RR soy), these are chimeric sequences (of viruses, bacteria, plants) which have been introduced using transgenesis to render the plant insect-resistant or herbicide-tolerant.

Transgenesis has been subject to a number of criticisms. The most fundamental question is that of the routine crossing of natural barriers to reproduction between species. The flows of genes from all kinds of sources that have been distilled by multiple laboratory processes could produce serious, totally unpredictable and uncontrollable systemic imbalances. Furthermore, transgenesis increases instability in how cells function due to the random location of the transgene inserted in the genome of the host organism: for example, it could be located in the middle of the native gene, rendering this gene inoperational. Moreover, an impaired transgene could produce a truncated protein.[10] This is why toxicology tests are conducted on transgenic plants bred for food and agriculture in Europe. A number of cases of disorders in the vital functions of populations of guinea pigs that have ingested these plants have been reported. Although GMPs clear tests and are sold and grown on a large scale, contradictory expertise exists in most cases.
Other threats of disturbances to the environment and agricultural systems have also become apparent. It has been amply demonstrated, for example, that transgenic crops cannot coexist with organic ones: organic maize farmers in Spain and organic rapeseed farmers in Canada who have seen their crops contaminated by transgenic plants from nearby fields have had to stop farming or switch crops.
To remove these obstacles without calling transgenesis into question, plant breeders have proposed both changes to techniques for modifying the genome and have also tried to ensure that the products of certain agricultural techniques using transgenic elements have not been considered as GMPs. In the first category, we have grouped together four techniques for direct intervention in DNA: cisgenesis*, random and site-directed mutagenesis*, nucleases,* and methylation*. In the second category, we present three particular agricultural and breeding techniques that use transgenesis: grafting, agro-infiltration* and inverse improvement*.

Changes to genome modification techniques

Cisgenesis: Transgenesis within the species

Genetic engineering is an attractive tool for plant breeding when one wishes to recover a specific gene, such as that which controls resistance to a pathogen in an heirloom variety or related species, to introduce it rapidly into a commercial variety. In perennial plants, such as fruit trees, this transfer using classic traditional breeding methods via repeated crossbreeding takes more than a decade. For this reason, cisgenesis[11] has been developed in a number of laboratories. In principle, cisgenesis is a technique equivalent to transgenesis apart form the detail that the gene to be inserted is from a plant from the same or a related species to that to be genetically modified. In theory, genes could be transferred naturally via sexual reproduction.

Because the genes of the plant introduced by genetic modification could in theory have occurred naturally in the cultivated plant, researchers maintain that the plant can no longer be considered a GMO. Therefore, the products of cisgenesis should not be required to be examined as genetically modified products. However, the position of the insertion of DNA transferred into the genome of the host plant using this technique remains unpredictable. Moreover, the expression of a gene in a GM product is always uncertain, and can have an undesired effect on the expression of other genes. The uncertainties associated with the random insertion of the cisgene, resulting in the extinction of native genes or even the production of truncated proteins, are the same as those posed by transgenesis.

Thus, while cisgenesis does not have the chimeric element of transgenic GMPs, it does not resolve the issue of the random insertion of the gene and the resulting threat of instability this poses to the transformed plant.

Mutagenesis: An increasingly targeted random modification

Mutagenesis is a genetic modification technique that was initially excluded from the scope of European directives on GMOs. It is an old technique (the initial trials were in the 1950s) in which breeders have invested heavily in order to improve it.[12]

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[10] These disturbances (the inhibition of a gene or a truncated protein) would not disrupt breeders, unless they affect the gene of interest. However, other disturbances to the genome can evade them, as well as experts responsible for evaluation.
[11] According to the report by the Dutch Institute of Food Safety (RIKILT): "Food and feed safety aspects of cisgenic crop plant varieties" (http://ikregeer.nl/document/blg-74631).
[12] Bayer has announced that it has sold mutated wheat and rice since 2001. It has also indicated that it has sold mutated maize and rapeseed since 1995, and mutated soy in the United States, Argentina and Turkey since 2003 (see note 12). For its part, BASF has developed different varieties of maize, sunflower and Clearfield rapeseed, rice, soy and wheat, which are protected by patents held by BASF and subject to proper use agreements. All are tolerant to herbicides that

The aim of mutagenesis is not to create a new gene, but to modify existing genes. Genetic mutations occur in existing organisms naturally; they are actually one of the most important mechanism in the variability of living systems that allows species to evolve and to adapt to their changing environments. These mutations appear when the cell replicates its DNA. The use of chemical products such as ethyl methanesulfonate (EMS) and physical agents known for their mutagenic properties (X-rays or UV rays) mimics this phenomenon, but considerably increases the rate, scope and concomitance of mutations.
The main problem with mutagenesis is that it causes mutations in DNA sequences in a totally uncontrolled manner. The vast majority of mutant plants yielded by mutagenesis are not viable. The essential task is to find mutated specimens of interest. Efforts to enhance the technique will therefore focus on two aspects: identifying the nature and location of mutations more precisely and rapidly, and refining the guidance system for specific target sequences of the genome.

Thus, when random mutagenesis is used, mutations can now be readily identified using Marker-Assisted Selection (MAS). This is the technique called TILLING (Targeting Induced Local Lesions IN Genome), which combines random mutagenesis via the use of a chemical product with a rapid and accurate selection and identification of resulting mutations. It also describes the phenotypes of plants produced by these cells containing mutations.[13]
The use of random mutagenesis is already widespread; a joint FAO-International Atomic Energy Agency (IAEA) programme lists mutated varieties in a database. With close to 2,500 mutated varieties recorded, this database is not exhaustive, as reporting is voluntary. Since mutagenesis is not subject to any binding census or labelling obligations, a number of mutated varieties are now sold openly without the knowledge of users, gardeners or farmers being aware of this.

The aim of new technical developments such as site-directed mutagenesis, which will consist of introducing mutations into a known target gene whose activity is to be modified, is to increase precision. To do this, part of the DNA sequence of the gene in question is replaced with another sequence defined for the experimental purposes. This sequence can be chemically synthesised in the case of relatively small portions, we then talk about oligonucleotide-directed mutagenesis* (a small DNA sequence of several dozen nucleotides). The oligonucleotides introduced into plants cells can replace the targeted portion of DNA thanks to a mechanism called homologous recombination. The latter is a universal mechanism for repairing DNA, and is present in living systems ranging from bacteria to mammals. Under normal conditions, it allows a cell to repair a damaged chromosome by copying information destroyed by the split onto another (naturally occurring) identical DNA molecule, the sister chromatid. This process can restore all initial information lost without introducing any mutations, or use synthesised oligonucleotides to introduce the mutation into the genome.
Applications of mutagenesis directed by oligonucleotides are actively being developed. In late 2010, for example, Cibus was conducting field trials in the United States, on canola modified to resist sulfonylurea herbicides. In July 2010, Cibus signed an agreement with BASF to introduce herbicide tolerance in BASF varieties of rapeseed and canola.[14]
In terms of risks, random mutagenesis appears to be an uncontrolled mechanism, since the nature, location and number of mutations generated are not controlled *a priori*. Physical and chemical products used to generate mutations significantly increase the number of genetic mutations or rearrangements in a cell, some of which are not identified.
Nevertheless varieties produced by random mutations are marketed without any specific evaluation. Millions of mutated plants are therefore introduced into complex biological systems, i.e. fields and their environment and, as we have seen, without regulation or traceability.
Oligonucleotide-directed mutagenesis is still very experimental: scientists do not know exactly how things occur[15] [16]. However, this gap in experts' knowledge itself is not the only problem. The synthesised sequences introduced can, in fact, no longer be identified as of the first cell multiplications, which eliminate any possibility of distinguishing a natural mutant from an artificial mutant protected by a patent through analysis. Industrial patents are more difficult to defend and the responsibility of the manufacturer harder to confront in the event of a problem.

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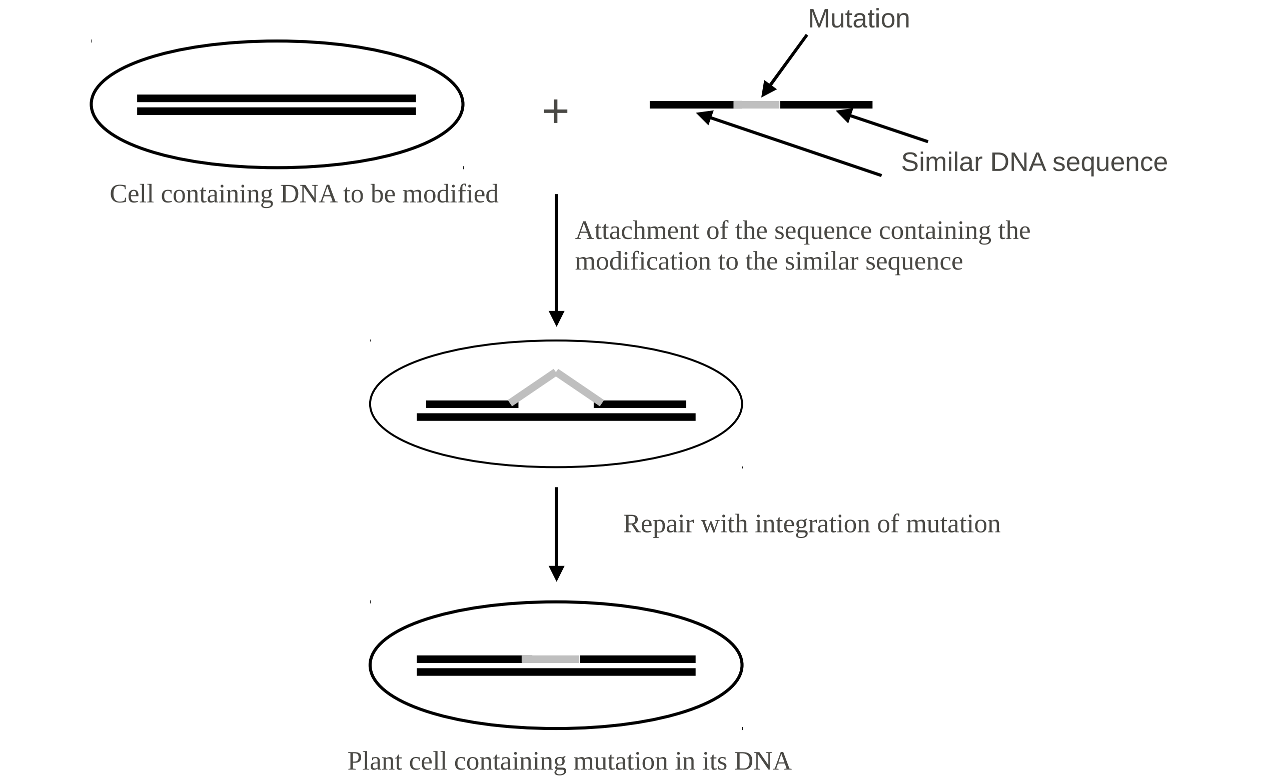
contain certain active ingredients, such as imidazolinone. BASF also sells varieties of mutated sunflower, lentils and even rice. Pioneer Hi-Breed sells varieties of Argentinean canola (Brassica napus) that are tolerant to herbicides or have high oleic acid content, as well as a variety of maize (Zea mays L.) that is midazolinone tolerant. Syngenta sells a mutated variety of maize that is tolerant to herbicides.
[13] Boualem A. et al., "A Conserved Mutation in an Ethylene Biosynthesis Enzyme Leads to Andromonoecy in Melons", Science, vol. 321, no. 5890, 2008, pp. 836-838 - "A transposon-induced epigenetic change leads to sex determination in melon", Nature, no. 461, 22 October 2009, pp. 1135-1138 - Piron F. et al, "An Induced Mutation in Tomato eIF4E Leads to Immunity to Two Potyviruses", PLoS ONE 5(6):e11313.doi:10.1371/journal.pone.0011313
[14] Meunier, E., "Nouvelles plantes mutées brevetées: des GMP qui cachent leur nom", Inf'OGM, no. 109, March -April 2011, http://www.infogm.org/spip.php?article4754
[15] Kochevenko A. et al., "Chimeric RNA/DNA Oligonucleotide-Based Site-Specific Modification of the Tobacco Acetolactate Syntase Gene", Plant Physiol, vol. 132, 2003, pp. 174-184.
[16] Beetham P.R. et al., "A tool for functional plant genomics: Chimeric RNA/DNA oligonucleotides cause in vivo gene-specific mutations", PNAS, vol. 96, no. 15, July 20, 1999, pp. 8774-8778.

Fig 1 : Mutagenesis



In short, both types of mutagenesis facilitate mutations within a much shorter period of time than spontaneous mutations in nature. In the laboratory, this technique frees itself of the "natural" mutation regulation by the environment in which these mutations occur. Ultimately, the thousands of mutated plants introduced into the environment have not been bred by the natural environment, (based on their local adaptation) and due to the stability of rearrangements caused by mutagenetic stress over time.

Meganucleases and zinc finger nucleases*: Precision scissors for DNA

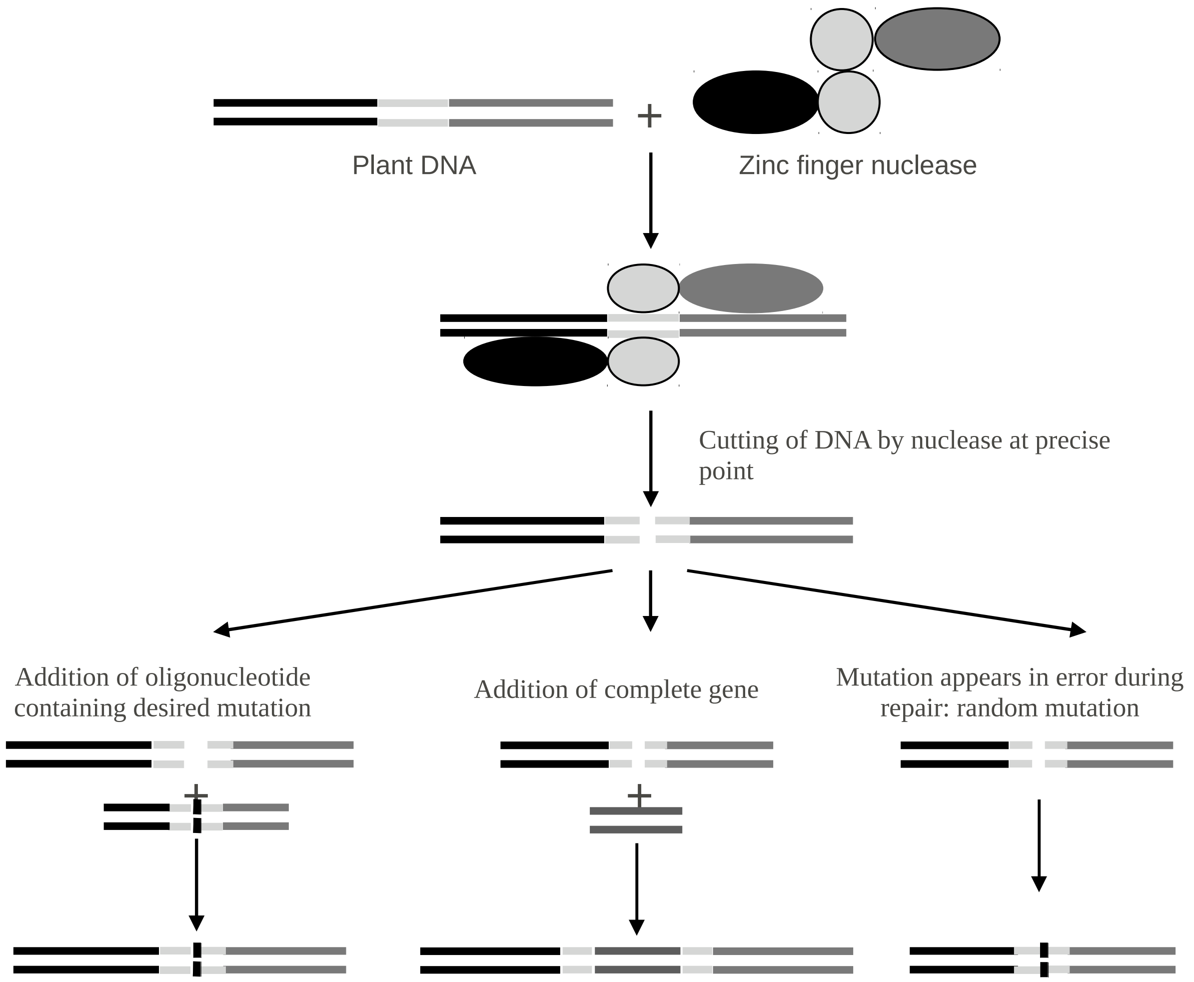
One of the disadvantages of traditional transgenesis techniques is that the transgene incorporates itself anywhere in the genome of the host plant, and can therefore affect its characteristics. The techniques described here involve enzymes and nucleases, which are DNA scissors. Nucleases cut DNA at several precise points on the molecule whenever they encounter a defined sequence. New types of enzymes called meganucleases* and zinc finger nucleases* can identify a unique cut site in the genome. As this break in the genome triggers a system that repairs DNA via homologous recombination between the cut site and foreign DNA inserted into the cells of the plant, the foreign DNA is integrated at a specific point on the genome chosen by the experimenter. Meganucleases are naturally-occurring enzymes, whereas zinc finger nucleases are created in a laboratory. The technique can also be used to improve traditional transgenesis and to introduce directed mutations into the plant genome.[17]

These techniques were developed to reduce the uncertainty associated with traditional transgenesis caused by the random insertion of synthetic DNA into the genome of the host organism. However, scientists recognise that in some cases, this does not prevent random insertion occurrence. Therefore, modified cells must still be selected *a posteriori* even if it is facilitated. Moreover, in general the technique requires the introduction of an encoding transgene into the cells of the host for the cutting enzyme. But we do not know what becomes of this gene: is it randomly integrated into the genome, or does it remain a vector that will then be lost? If it is integrated, can it be reactivated in an uncontrolled manner? Might it not mutate and change its specificity, resulting in random cuts in the genome? This last hypothesis is confirmed by the toxicity found in certain cases: scientific literature highlights the existence of toxic zinc finger nucleases, with this toxicity probably due to cuts in places other than in the target sequence. Strategies to reduce or avoid this toxicity are currently being researched. The phenomenon clearly demonstrates that specificity is not

[17] Meganucleases are used in several areas in both the plant and animal worlds. As a result, Cellectis has announced on its website that "BASF, Bayer Cropsciences, Pioneer, Limagrain and Monsanto already use Cellectis technology", which consists of meganucleases. Meanwhile, in November 2010 Precision BioScience Inc signed a partnership agreement with BASF with a view to generate and sell mutated plants obtained using Precision BioScience Inc meganucleases. Zinc finger nucleases are also experiencing a boom; there are plans to use them in several fields, ranging from genetic therapy in humans to the modification of the plant genome.

guaranteed, and that the technique can still result in cuts elsewhere in the target sequence. (See diagram below)

Fig 2: Zinc finger nuclease



Graphic inspired from: “Zinc finger nuclease technology heralds a new era in mammalian Transgenesis”, Le Provost et al., 2009, Trends in biotechnology, Vol. 8, no.3, pp.134-141

Methylation can be used to switch off genes

It is also possible to act on genetic expression without intervening directly in the DNA sequence by inserting molecules that can partially but permanently block a given characteristic. DNA methylation is a process that intervenes naturally in epigenetic phenomena that result in reversible hereditary changes in the expression and functioning of genes, without altering the DNA sequence. Thus, the methylation of a DNA sequence modifies the expression of one or more genes by altering not the sequence itself, but the number of chemical molecules - methyle radicals* - attached to this sequence. These methyl radicals can be introduced artificially via the introduction of an RNA that matches the gene to be switched off, or even a particular transgene that allows the synthesis of this RNA. The RNA then triggers methylation in the cell of certain plants and the targeted gene will no longer express itself.

These new profiles of expression, which therefore depend not on the DNA sequence but on their "state", can be passed on from one generation to the next if the sequence concerned is found in germ cells. Thus, this technique can be used to modify the phenotype of a plant without modifying its genetic sequence. Unexpectedly, if we follow the principles of traditional genetics, it has been demonstrated in a rapeseed population that individuals could be genetically identical but possess different physiological and agronomic characteristics.[18] These differences are the product of epigenetic characteristics that open up new paths for researchers for the breeding and improvement of plants that have hitherto been little explored.

Methylation is a product of a new field of research in biotechnology, acting on the environment of the genome without directly affecting the DNA sequence. It remains highly intrusive (introducing synthetic RNA molecules) and experimental, with little evaluation to date of the risks of instability.

[18] Hauben M. et al., "Energy use efficiency is characterized by an epigenetic component that can be directed through artificial selection to increase yield", Proc Natl Acad Sci USA, 2009 Nov 24,106(47), pp. 20109-20114.

The main lesson to be learnt from our knowledge of methylation is that the environment of the genome can modify genetic expression permanently. At the very least, this could radically alter technophiles' views of how a cell and an organism operate, a view that is based on a reductionist approach to genetics, limited to the DNA sequence.

Specific agricultural and breeding techniques that use transgenesis

European experts must also assess agricultural and selection techniques that partially use transgenesis, or some part of the process. Some of these techniques, such as grafting, are very old. What is new here is the grafting of a non-GM scion onto GM rootstock, and therefore to determine the nature of the grafted plant. Other, more recent techniques indirectly introduce transgenesis in a number of ways. In the case of agro-infiltration*, for example, it is not the plant itself that is transgenic, but an infectious, non-pathogenic bacterium that is genetically modified to stimulate production of a particular protein. The plant then plays a supporting role. Another breeding technique, inverse improvement*, sees the involvement of transgenesis at certain stages but these transgenes are no longer present in regenerated plants that will be marketed.

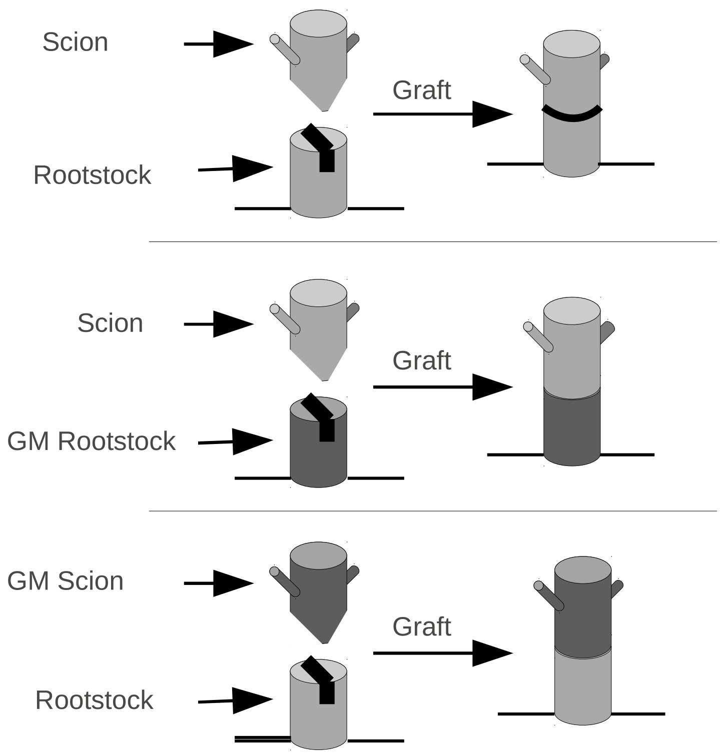
Grafting: The transmission of genetic modification via GM rootstock

Plant grafting is a very old gardening technique that is very widely used in viticulture and for fruit trees. Grafting consists of naturally fusing a plant organ (the stem or shoot), called a scion, onto the stem of another plant that can be of a different species, the rootstock. To combat certain diseases common in industrial monocultures, breeding programmes consist of adding non-transgenic scion of conventionally-bred varieties to transgenic rootstock. The reverse is also possible, with transgenic scions added to non-transgenic rootstocks.

Thus, the question is to determine whether the characteristic of the transgene carried by the rootstock or the scion is found in the whole plant or not. More than a decade ago, researchers at Inra in Versailles revealed the possibility of such a transfer in the case of tobacco (Palauqui et al, 1997, The Embo Journal). This possible transfer of products from the transgene of a rootstock to a scion has been confirmed by more recent scientific work, but for all that these works do not show the passage of the transgene itself.[19]

The best-known use in France is the field trial conducted by the Colmar INRA in Alsace on stocks of transgenic vine destroyed by reaping. These vines had been genetically modified to resist the grapevine fan leaf virus carried by nematodes. The field trial was authorised within the framework for legislation on the dissemination of GMOs; therefore, it would seem to have been agreed by Inra and the regulations that the rootstock remained a GMO. As far as the whole plant itself is concerned, experts still seem very prudent in their opinions. Thus, in a publication dated 15th March 2010 on this test, the scientific committee of the High Council for Biotechnologies (HCB) notes in relation to this test that "in the absence of knowledge on the transfer of products from the transgene of the rootstock to the scion, the non-transgenic scion is subject to the same measures as products that are transgenic from the outset: flower buds shall be destroyed before flowering and the products of pruning and trimming shall be incinerated".

Fig 3: Grafting



[19] Dunoyer et al., Science, 2010; Molnar et al., Science, 2010; Buhtz et al., BMC Plant Biology, 2010.

Agro-infiltration: The plant, factory for a modified bacterium

It is easier to produce a new protein for industrial and/or pharmaceutical purposes from a genetically-modified bacterium than from a plant whose genome is more complex and more difficult to transform. On the other hand, cultivated plants can, in some cases, be used as a factory by GM bacterium to produce a given protein on a larger scale. The technique of agro-infiltration uses the genetically modified bacterium *Agrobacterium tumefaciens* to infect whole plants without being pathogenic. The genetic construction of interest, inserted into A. tumefaciens beforehand, can then be transferred into a greater or lesser number of the cells of the plant that will produce the protein of interest, without integrating the genome of the host plant. This technique is now on the list of new techniques, as its use has been adapted to obtain greater quantities of transgenic proteins.

Infection can occur in one of two ways. One is via the use of a solution in which plants are soaked. In this case, all the cells of mature leaves on the plant (except for those in the process of formation) are infected and end up expressing the protein of interest. This is referred to as magnifiction.[20] The other method involves the application of a solution sprayed directly onto plants in the field. In this case, the solution also contains an abrasive product that damages the plant cell wall and allows bacteria to infect the plant. The plants then take two to three weeks to express the genetic construction introduced into most of their tissue. In both cases (plants that have been soaked or sprayed), the genetic construction has not been integrated into the genome of the infected cells, with the modified viral sequences in the bacterium constituting independent replication units (replicons).[21] Thus, the transgene is not passed on to the next generation. Used mainly to produce proteins for pharmaceutical purposes, these two techniques differ in the objective of a more or less widespread production of proteins of interest, with the company Nomad proposing a technique that can produce up to one tonne of proteins per hectare under cultivation.

As part of the dissemination of *A. tumefaciens* modified in the field, several questions arise for which there is no answer as yet. Thus, the probability of the plant forming seed that may or may not contain the virus-protein construction of interest is poorly understood, but *a priori* not zero. In this case, there could be a transmission of the plant to subsequent generations and the plants produced will therefore become GMPs. In addition, the extent of the presence of modified A. *tumefaciens* in the environment is not known.[22] Yet fields of crops are sprayed on a massive scale with a genetically modified bacterium without monitoring the infection of plants around these fields, unless the areas covered by the crop are so extensive that only the centre of the field needs to be sprayed.

Reverse breeding revives the parents of hybrid plants

An increasing number of plant breeding techniques use transgenesis. At times, transgenesis is used during one phase but the transgene is not preserved in subsequent phases, and will not be found in the plant put on the market. One highly sophisticated technique for breeding hybrids, reverse breeding, is now under evaluation by European experts.

In the modern breeding of industrial plants, the most widely-used technique is that which produces hybrids by crossing "pure" lines. These hybrid varieties, known as F1 varieties, cannot be reproduced by farmers in their fields, since these varieties do not retain their genetic structure. And as they can only be reproduced via the specific crossing of the parental lines of these F1 varieties, the latter are jealously protected from competition by breeders. Reverse breeding aims to identify the parents of hybrid plants with the desired characteristics. In their analysis of the ability of certain plants to reproduce without fertilisation, scientists have discovered how to inhibit or "control" the natural genetic mixing that occurs during cell division, known as meiosis, which is referred to as modified meiosis or apomixie*. Modified meiosis is achieved in various stages with the use of chemical products or known mutants in genes involved in meiosis, or even by adding a transgenic sequence. One point worthy of note is that if a transgene is used to modify the meiosis, the latter will not be present in the regenerated plant. This technique is not yet used commercially in plant production, but companies aim to be able to rediscover the lineage of parents to produce F1 plants using this method.[23]

Reverse breeding based on blocking the genetic mixing that occurs during cell division affects one of the key elements in evolution, and this approach strengthens the questions relative to the normalisation of varieties sold. On the one hand, plants are deprived of their ability to generate variability within their population, reducing their "natural" adaptation to their environment; on the other hand, these plants, which have been normalised since the transgene has been suppressed, have undergone profound genetic transformations that combine different techniques based on the use of chemical products, mutants or transgenes whose effects have not been evaluated.

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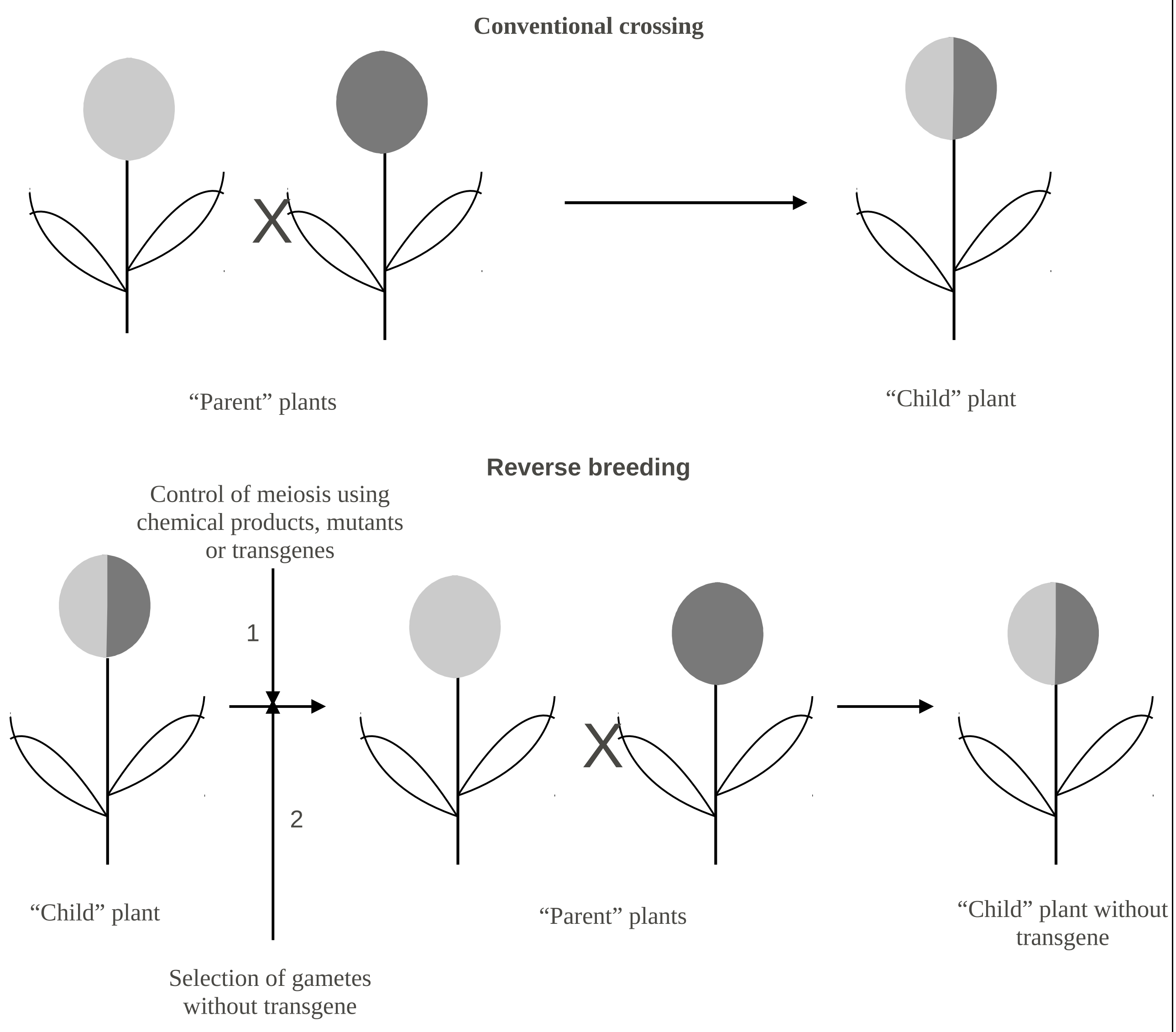
[20] Marillonnet S. et al., "Systemic Agrobacterium tumefaciens-mediated transfection of viral replicons for efficient transient expression in plants", Nature biotechnology, vol. 23, no.6, 2005, pp. 718-723.

[21] Gleba Y. et al., "Viral vectors for the expression of proteins in plants", Curr. Opi. In Biotech., no. 18, 2007, pp. 134-141.

[22] Response from Yuri Gleba to a question at the HCB seminar held on 1-2 December 2010.

[23] Wijnker E. et al., "Managing meiotic recombination in plant breeding", Trends in Plant Science, Volume 13, Issue 12, 23 October 2008, pp. 640-646.

Fig 4: Reverse breeding



Summary presentation of each technique

Technique	Nature of sequence used	Insertion in genome?	Targeted/random insertion	Heritability	Probable opinion of European experts
Transgenesis	Transgenesis (Promoter + gene of interest from sexually incompatible organism + terminator)	Yes	Random	Yes	GMO already recorded
Cisgenesis	Cisgenesis (Promoter + gene of interest from sexually compatible organism + terminator)	Yes	Random	Yes	GMO but outside scope of law
Mutagenesis via oligonucleotides	Oligonucleotides	Yes	Targeted	Yes	GMO or not GMO but outside scope of law
Mutagenesis via meganuclease	Oligonucleotides	Yes	Targeted	Yes	
Mutagenesis via zinc finger nuclease	Oligonucleotides	Yes	Targeted	Yes	GMO but outside scope of law (except if complete gene is inserted)
DNA methylation	Transgene	Yes	Random	Yes	GMO or not GMO but outside scope of law
Grafting (GM rootstock)	Transgene / Cisgene	Yes	Random	No	GM plant / fruits, non-GM seeds (if scion is not GM)
Grafting (GM scion)	Transgene / Cisgene	Yes	Random	Yes	GM plant
Agro-infiltration	Transgene in an independent construction of the genome	No (except if viral DNA + transgene)	No insertion	No	GMO / Not GMO
Reverse breeding	“Natural” mutant or transgene	Yes	Random	No	GMO / Not GMO

General considerations in relation to new techniques for the genetic modification of plants

With a brief explanation of the principles of new technologies for the genetic modification of plants, the man in the street can make several observations in relation to the current development of biotechnologies used in plant breeding.

First of all, we can but be amazed by the astounding speed of biotechnological innovation and the complexity of processes; just as we have familiarised ourselves with certain modifications and attempted to analyse the associated risks, these modifications are replaced by new techniques. However, this sentiment is soon tinged with a sense of indignation at the repeated headlong rush to produce increasingly artificial systems inserted in plants grown for agriculture and food: there is no recognition for the extent of public opposition to GMOs. At this point, we could acknowledge the technological exploits of molecular biology and the results of fundamental research that they could produce; but, as we are well aware, the return on investment is expected elsewhere: in the development of elite plants that will be cultivated in the future on hundreds of thousands of hectares. These research efforts are financed by laboratories to be applied to plant breeding and produce plants in uncontrolled environments.
And in spite of their differences, these techniques have a number of points in common.

Reductionism as a credo

The conceptual framework for experiments is still most often the product of an approach that has long been criticised as reductionist, as it only considers the living system in its genetic and molecular aspect, an aspect which itself is often limited, as indicated earlier, to an old dogma that no longer stands: "one gene - one protein – one function". As we have seen, most techniques for the genetic modification of supports for heredity are conducted on the cell, and not on the whole plant. When the DNA of the cell has been modified, the plant is regenerated using other laboratory techniques, multiplication in test tubes via in vitro culture, then the greenhouse cultivation before the experimental field trials. This creates new conditions that are very far removed from natural reproduction and farming modes at each stage.

Technical solutions for moving beyond transgenesis

New techniques for the modification of plant DNA often aim to correct, conceal or respond to the limitations of and errors in earlier techniques, such as transgenesis, which was but a prelude to the techniques to come. For example, it is the excessively random nature of the first forms of mutagenesis that encouraged researchers to focus on transgenesis, in order to "enhance precision". The exponential progress made in molecular marking, however, now means that it is possible to monitor the "random" mutagenesis mechanism with greater precision, without the need for several generations of cell multiplications and multiplications of plants in order to be able to measure its effects, as was the case thirty years ago. Research into transgenesis is at the heart of this progress in molecular marking. It has thus made its main "rival" technique, mutagenesis flavour of the day, a flavour which it must soon replace: the number of new

varieties the product of site-directed mutagenesis available on the market is now catching up with these new transgenic varieties.
Industrial investment in new site-directed mutagenesis techniques that to a large extent suppress its random nature has caught up with much of the investment in transgenesis. Transgenesis is no longer just a tool in a box of tools that is becoming ever more diverse. The performance of these toolsoften improves when they are combined.

Avoiding the evaluation framework
All of these new techniques have been developed to create GMOs without these organisms being considered as GMOs in the eyes of the law. The companies that spend considerable sums on developing these procedures have every interest in doing so if they wish to avoid procedures for the evaluation of GM plants. The legal framework that influences potential returns on investment in research and development becomes an essential factor that determines the technique(s) chosen by businesses for development of a given technique. At present, this manifests itself in three at times contradictory priorities:

- Setting rules for access to the market whose costs and constraints favour the creation of monopolies, but also certain techniques and monopolies at the expense of others. Tensions in relation to European regulation, which for 20 years have affected transgenesis alone, while ignoring other genetic engineering techniques, demonstrate how manufacturing strategies fit into, and affect, debates on regulation (for example, European companies such as Bayer have favoured breeding plants that are herbice-resistant through mutagenesis and that are not considered GMOs under European regulations);
- Protecting industrial patents on elements that can be easily identified using simple methods of analysis and that remain stable for as long as possible through successive multiplications or recombinations of living organisms;
- Research into non-identifiable genetic modification techniques that create products that can be presented as "traditional" to consumers who resist uncontrolled attacks on the natural equilibria of living organisms.

Yet, given the extent of ignorance among nano-engineers of the functioning of the agro-ecosystems to whose disruption they shall be contributing via the risks associated with the new techniques referred to in this brochure, we can find the same potential imbalances in the living systems inherent to plants that have been transformed by transgenesis. As a result, we believe they should all be included within the scope of the regulatory framework on the biosecurity of GMOs.

2. Evolution of intellectual property rights to modified plants

A significant proportion of investment in plant biotechnology research is allocated to genetic engineering and the molecular marking of varietal innovation. Plants are modified in the depths of their genome in a sufficiently discreet manner for them to avoid regulatory frameworks on the biosecurity of GMPs, while at the same time being exposed to the same approaches to appropriation via industrial property rights.[24] In this way, new techniques create new rules for market access that benefit some businesses and are detrimental to others. Indeed, these rules can result in the exclusion of techniques that are the product of popular knowledge and accessible to people, such as the determination of varieties cultivated according to traits that are easily identifiable in fields to the exclusive benefit of techniques that are accessible only to businesses with the capital necessary to implementing them, such as the identification of varieties according to molecular marker. Thus, forms of industrial property will adapt to changes in techniques, at times competing with each other but often mutually legitimising and reinforcing each other.

In the plant breeding sector, the consolidation of the seed market continues. In 2008, it was controlled by nine companies: Monsanto, Syngenta, Dupont, Limagrain, Dow Agrosciences, KWS, BASF, Bayer and Land O'Lake. A study by Philip H. Howard of the University of Michigan on the period 1996-2008 illustrates this consolidation. Above all, this study clearly demonstrates that the international seed market is now dominated by chemicals and pharmaceuticals companies that have acquired seed companies (in full or in part) already present in the market, with some of these acquired companies having already taken over other seed companies, which in turn owned other seed companies[25])

The take over of plant breeding by chemicals sector will have two major consequences: firstly a trend towards the production of plants dependent on other chemical products developed by the company, the best-known example being the famous transgenic soy plant that is tolerant to Monsanto's Round-Up herbicide; and secondly the greater investment in molecular transformation and the appropriation of plants through patents. This strategy to conquer the market will come up against the interests of traditional seed companies, which have built their monopolies on another system of industrial property: the New Plant Variety Certificate (NPVC) (see box below).

Whether on an international, European or French level, these industrial property rights on plant varieties and seeds are regulated by different laws, conventions, treaties and accords. An exhaustive explanation of these different regimes would require a separate volume of its own. Here, we will merely present them in diagrammatic form (see p. 19) – with the inherent limitations associated with this presentation – in order to summarise this complex system.

What we are interested in going here is identifying the role of the actors in this Monopoly ofliving organism-grabbing. How will new techniques be included in these frameworks on industrial property? How will they contribute to amending them? What scope do farmers and gardeners now have vis-à-vis to use seeds? An explanation of these issues is proposed based on two testimonies.

To help understand the evolution of the strategies adopted by business in relation to patents, the speech by of François Meienberg as part of the "No patent on life" community campaign analyses the claims made by businesses when filing for patents at the European Patent Office, and provides a few keys to current trends. Guy Kastler"s speech provides the perspective of farmers, with an analysis from the Semences Paysannes Network based on the analysis of changes in property rights to seeds in Europe and elements on the games played by manufacturers in the drafting of the new European legislative framework.

The two main forms of industrial property of plants

Patents: A patent granted to an individual or legal entity constitutes an industrial property right to an invention. The patent provides an exclusive right of exploitation, authorising the holder to prohibit third parties from exploiting the patented invention. An "invention" meets three fundamental criteria: novelty (no information on this invention was available prior to the application for a patent), inventiveness (the conception of the invention should not be obvious to an expert in the given field) and the possibility of industrial application (whether for manufacture or for use). Once granted, the patent requires that the whole invention be made public (to ensure that it can be replicated once the patent has expired). While the period of validity of a patent may vary, it is generally twenty years. Finally, patents are only valid on territories covered by the structure that has issued the patent.

In Europe, patents are granted and managed by the European Patent Office (EPO). Created upon the signing of the

[24] We will use the term "industrial property" rather than intellectual property when referring to plants or living systems, unless we are referring to citations. The term "intellectual property" encompasses the protection of creations of the mind through copyright, for example, and innovations that must necessarily have an industrial application. Given that claims to intellectual property over a living being are highly questionable, we prefer to refer to the source of their legitimacy: the industrial development of a technique or process while providing legal protection for a monopoly on an innovation.

[25] Howard P., "Visualizing consolidation in the global seed industry: 1996 - 2008", Sustainability, no.1, 2009, pp. 1266-1287

European Patent Convention by a number of European countries in Munich in 1973,[26] the EPO is not under the control of the European Union; it is a multinational organisation whose management is appointed by its member States, but which does not have a political structure of governance to which these managers must report. Note that the European Union has introduced specific legislation for "the legal protection of biotechnological inventions" (Directive 98/44).[27]
For the specific area of plants, there is a fundamental difference between the US and European patent systems: In the United States, genes, plants, processes for breeding new varieties and varieties themselves can be patented, whereas in Europe, only genes and certain processes for breeding new varieties can be patented. Industrial property of varieties is exercised by the rules of the New Plant Variety Certificate of the UPOV.
Plant variety rights: Discussed at a conference held in Paris in 1961, the International Convention for the Protection of New Varieties of Plants ("the UPOV Convention") has now been ratified[28] by 69 countries. The objective of the UPOV is to ensure "the international recognition of the rights of plant breeders". Thus, this convention provides "a sui generis form of intellectual property protection which has been specifically adapted for the process of plant breeding and has been developed with the aim of encouraging breeders to develop new varieties of plants",[29] a system that consists of the issue of a New Plant Variety Certificate (NPVC). Four main conditions must be met in order for a NPVC to be issued for a variety. The first three criteria ("DUS") are those relevant to listing in the catalogue of varieties: it must have characteristics that (i) distinguish it from known varieties; (ii) are uniform within a population of plants of the same variety; and (iii) are stable over time. The fourth criterion is novelty. Originally, the characteristics in question were exclusively phenotypical but, since 1991 and the review of the UPOV, they have been characteristics that are the product a genotype, or of a combination of genotypes.

Different levels of regulatory framework for industrial property for plants

International level :

UN = The genetic resources that are the product of biodiversity are placed under the sovereignty of States. States can authorise companies to use them in exchange for benefit sharing. => Convention on Biological Diversity (CBD)

FAO = Biodiversity should be protected, but companies must have access that is as free as possible to all agricultural genetic resources. Plant resources associated with food and agriculture are thus the product of the CBD. => **International Treaty on Plant Genetic Resources for Food and Agriculture (ITPGRFA).** Contains the recognition of farmers' rights.

WTO = All States must have a system in place for the protection of inventions, including those that relate to plants. => **Trade-Related Aspects of Intellectual Property Rights (ADPIC)**

A hundred countries have come together to adopt a system for the protection of new varieties of plants, different to the patent. => **Union for the Protection of New Varieties of Plants (UPOV)**

UN = As a minimum, rules on the protection of intellectual property rights must be harmonised at international level. **=> World Intellectual Property Organisation (WIPO)**

European level :

European Union - Directive on the legal protection of biotechnological inventions. => **Directive 98/44** – A patent system for the European Union is currently being established within this framework.

European Union – Regulations to implement the 1991 UPOV convention. => **Council Regulation 2100/94 (amended by 1768/95)** – This regulation puts in place the Certificate for the Protection of New Varieties of Plants according to UPOV regulations.

Europe (47 countries, including the 27 in the EU) - Text establishing rules for the issue of patents in particular on genes and plants. => **European Patent Convention** – Established the European Patent Office in Munich. Patents issued are applicable, on request, to all or some of the 47 signatory states. Patents on varieties are not possible.

[26] http://www.epo.org/patents/law/legal-texts/html/epc/1973/e/contents.html
[27] http://eur-lex.europa.eu/smartapi/cgi/sga_doc?smartapi!celexplus!prod!CELEXnumdoc&lg=FR&numdoc=31998L0044
[28] http://www.upov.int/export/sites/upov/fr/about/members/pdf/pub423.pdf
[29] http://www.upov.int/

French level :

France - Protection of new varieties of plants according to UPOV regime of 1970. => **French Plant Variety Protection Certificate**. Currently undergoing reform to align with UPOV 1991

France – Direct application of Council Regulation 2100/94 on the Community New Plant Variety Certificate. => **Community NPVC in France**

France - The issue of national patents via the Institut National de la Propriété Intellectuelle. => **French patent on genes or technology for obtaining new varieties (little used due to existence of European patent)**

A new European framework for plant patents

François Meienberg, Bern Declaration

The purpose of patents is to promote innovation, to be a driving force for innovation by establishing legal monopolies. But the correlation between patents and innovation follows an upward curve at a certain level of protection, and a downward curve after an "optimal" level of protection. Beyond this point, protection hinders innovation. Therefore, all States are obliged to manage their position on this curve, lest they see a decline in innovation at national level.

For States, this policy of innovation should not necessarily take precedence over other policies, like respect for human rights, the protection of biodiversity (according to the convention on biodiversity), and even the rights of farmers, breeders and consumers – the right to food. In agriculture and food specifically, such are the ties between the various components (farmers, breeders, consumers, biodiversity) and intellectual property, that modifications to one element affect all others.

The report by the Special Rapporteur for the United Nations,[30] Olivier de Schutter, recalls that States have an obligation to respect the right to adequate food. Within this framework, the implementation of legislation or measures that hinder farmers' access to an informal seed exchange system could be in breach of this principle, as it could deprive farmers of a means of making their livelihood. Two other passages in the report are fundamental to an understanding of patent issues in the area of food: "States have an obligation to protect the right to food", by legislating on the activities of patent holders and breeders in order to prevent any violation of the right to food of farmers dependent on these elements, to enable them to continue tilling the soil and "States have an obligation to fulfil the right to food [...] by actively reinforcing access to the resources and the means required to ensure their subsistence". Once in place, it was found that no common system for all States in the world could fulfil these obligations. So in 1999, the IPGRI (International Plant Genetic Resources Institute) established that "the ideal *sui generis* system that would meet the needs of all countries does not exist". And in 2002, the British Commission on Intellectual Property Rights indicated that "Given that patents can impose restrictions on the use of seeds by farmers and researchers, developing countries should not, in principle, issue patents on plants and animals, which is allowed under the Treaty on ADPIC. Rather, they should envisage different *sui generis* systems for plant variety protection".[31] Based on the above, it would appear that the ADPIC and UPOV systems cannot function without becoming an attack on the right to food.

European frameworks for the protection of intellectual property

Intellectual property has been formalised in several frameworks. The international convention that oversees regulation in this area consists of the Treaty on Trade-Related Aspects of Intellectual Property Rights (ADPIC). This text, which was adopted as part of the WTO accords of 1994, has been signed by 120 countries. Article 27 states that patents shall be available for any inventions, whether products or processes, in all fields of technology, provided that they are new, involve an inventive step and are capable of industrial application". It should be noted that the notion of inventiveness is the most difficult to prove; it is the basis for 99% of challenges to patents that have been confirmed. The notion of "novelty", for its part, is enforced with particular rigour. Member States are not helpless in the face of the above, since article 27 goes on to state that "*Members may also exclude from patentability inventions, the prevention within their territory of the commercial exploitation of which is necessary to protect order public or morality, including to protect human, animal or plant life or health or to avoid serious prejudice to the environment*". Yet this provision is almost never used. Finally, article 27 contains an additional provision, the importance of which we will see later: " *Members may also exclude from patentability: b) plants and animals other than micro-organisms, and essentially biological processes for the production of plants or animals other than non-biological and microbiological processes. However, Members shall provide for the protection of plant varieties either by patents or by an effective sui generis system or by any combination thereof*".

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[30] "Le droit à l'alimentation, Politiques semencières et droit à l'alimentation: accroître l'agrobiodiversité et encourager l'innovation", Note of the Secretary-General, 23 July 2009.

[31] Executive summary and full report available at: http://www.iprcommission.org/graphic/French_Intro.htm

This international text has been implemented in the European Union as part of Directive 98/44/CE,[32] which in its article 4.1 addresses this notion of the non-patentability of plant varieties, since they are protected by another industrial protection system (the law on new plant varieties): "The following are not patentable: a) plant and animal varieties; b) essentially biological processes for the production of plants or animals". To illustrate the complexity of this specific point and the issues, details are provided in later parts of the text, details which warrant a mention her. Thus, article 4.2 states that "Inventions which concern plants or animals shall be patentable if the technical feasibility of the invention is not confined to a particular plant or animal variety". Meanwhile, article 4.3 states that, "Paragraph 1, point b) [article 4.1b] shall be without prejudice to the patentability of inventions which concern a microbiological or other technical process or a product obtained by means of such a process". All of the above would suggest – albeit with certain restrictions – that numerous methods for improving varieties, as well as plants obtained using these methods, could be patented in Europe.

Of course, these patents extend to all "biological matter" obtained from "biological matter" or the patented “process”. In the field of biotechnology article 9 is of particular interest, as it sets out what is covered: "The protection conferred by a patent on a product containing or consisting of genetic information shall extend to all material, save as provided in Article 5(1), in which the product in incorporated and in which the genetic information is contained and performs its function". In short: a patent on a gene and its function extends to any product that contains this gene and in which the function of the latter expresses itself.
Finally, the "privilege" of the farmer is assured in this text, with article 11.1 stating that " the sale or other form of commercialisation of plant propagating material to a farmer by the holder of the patent or with his consent for agricultural use implies authorisation for the farmer to use the product of his harvest for propagation or multiplication by him on his own farm ". In Switzerland, legislation has made much more specific provision for this type of case: article 35 of its Federal Law on Patents for Inventions states that "any accord that restricts or repeals the privilege of farmers in relation to foodstuffs and animal feed is null and void".

In Europe (in the geographical sense of the term, i.e. 38 countries, including the 27 countries of the European Union), the European Patent Convention is also an implementation text. The latter determines elements that can be patented for patents of the European Patent Office, aware that the same provisions as those of the European directive apply. Rights under a patent are set out in national legislation and apply equally to patents granted by the European Patent Office. The Office was created in 1977, when the European Patent Convention signed four years earlier came into force. The European Patent Office (EPO) handles all procedures associated with patents in Europe. The EPO Board of Directors, which is made up of representatives from Contracting States, exercises legislative powers for the Office, is competent on the political issues of the Office and oversees the activities of the Office. However, parting from general rules, national differences can emerge. Accordingly, a significant difference exists between French intellectual protection and its British equivalent in the area of chemical substances and proteins. In the United Kingdom, a patent on a gene means *de facto* coverage of all functions of proteins encoded by this gene, even if they are not described in the patent. In France, the gene patent only applies to functions in fact described in the patent.
In the EU as a whole, patent applications in the area of genetic engineering have been in decline for a number of years, with professionals in the agricultural sector opting for NPVC instead.

Business strategies: Research into patentable techniques
Nowadays, patents have an unexpected advantage of revealing the positions of companies in terms of the limitations of genetic engineering. Thus, according to Monsanto, "*success in improving plants using transgenic means is low due to the presence of a number of factors, including the unpredictability of the effects of a specific gene on the growth of the plant, the response of the environment, the low frequency of the transformation of maize, the absence of control over the gene once it is inserted into the genome and other undesirable effects of transformation events and processes of tissue cultures*".[33] Or, according to Syngenta, "*most phenotypical characteristics of interest are controlled by more than one genetic locus, with each contributing to varying degrees to this characteristic*".[34] In the case of the latter, it is the limitation imposed on biotechnologies by genetic functioning itself that is presented as a limiting factor by the company.
Thus, we have seen that plant varieties were not patentable as such. Therefore, companies have put "tools" in place that enable them to transform certain elements present in plants into inventions, and therefore to obtain patents whose protection extends to these plants. These tools include, for example, the quantification of components of the plant (fatty acids, proteins, etc.), the description of phenotypical characteristics (number of leaves, size of the plant, yield, growth, etc.), the detection of resistance to biotic and abiotic stress, the genomic analytical examination of genetic sequences present in nature, or even mutagenesis. Ultimately, all of these practices allow a patent to be obtained that, while it does not concern varieties, would despite everything allow companies to obtain intellectual property of plants, and furthermore that is relevant to all plants that will be affected by the procedure used or in which these protected

[32] Directive 98/44/EC of the European Parliament and of the Council of 6 July 1998 on the legal protection of biotechnological inventions", Official Journal L213 of 30.7.1998, pp. 13-21.
[33] Monsanto patent, no. WO2004053055, "Transgenic maize with enhanced phenotype".
[34] Syngenta patent, no. WO2008087208, "New maize plant".

characteristics might persist. To date, existing techniques that target DNA and allow patents to be obtained consist of DNA marking: this technology is not aimed at a specific region of the genome, but demonstrates the distribution of elements and general structures in the genome using identified markers. These tags, also called markers, are known DNA sequences that are generally short and repeated. The results will then be used to establish other comparisons and study correlations with certain phenotypical properties – market assisted selection (MAS): the correlation of specific DNA sequences with sought-after phenotypical properties. Thus, this method aims to find correlations between genetic markers and a genetic property (characteristics) that cannot be reduced to a single gene, since it is based on the interactivity of various parts of the genome. For companies, this work with markers produces the possibility to extend the protection provided by their patents to whole plants: the presence of a patented marker giving notice of ownership of the organism. However, on examining the Broccoli Case we will see that a plant breeding process that uses marker-assisted selection cannot be patented.

The example of the TILLING technique follows the same lines: the exposure of a plant to various sources of stimulation in order to produce mutations in the plant and its subsequent analysis to identify and locate these mutations, allows plants to be patented. Some people refer to biopiracy in the field, the biopiracy of biodiversity. The general principle consists of marking existing biological biodiversity using simple technical tools and, in doing so, reducing the biological diversity of agriculture (seeds, animals) that are accessible to all, by appropriating it through exclusive property rights. These tools could be particularly effective for appropriating the genetic resources of centres of biological diversity. Thus, laws on patents are deformed to allow the appropriation of the basic resources of world food production. Some specific examples illustrate the latter phenomenon of appropriation, which consists of demanding a more general application in the patent application. In its patent entitled "Compositions and methods of plant breeding using high density marker information", no. WO2008021413, Monsanto writes: "The methods of this invention can be used to improve any non-human organism. More specifically, these methods can be used to improve mammals, such as mice, pigs, cows and birds" (page 1037). Another example is that in its patent application WO2008121291, where the company states that "soy has a thin genetic base when compared to that of other cultures (...) As a result of this thin genetic base, soy is more likely to be affected by disease and attacked by insects. Exotic genetic resources possess resistance to disease, insects, nematodes and environmental stresses, etc. Breeders create bridges between cultivated and exotic genetic resources" (page 81).

The broccoli case

A patent application for broccoli filed by the firm Plant Bioscience Limited Norwich is currently being challenged in court. An examination of this case, that was filed by companies and Limagrain in particular, illustrates everything we have just seen in concrete terms: the avoidance of patent laws, the importance of existing legal definitions, and the approach of companies themselves in these areas.

The company entitled Plant Bioscience has obtained a European patent (EP 1069819) on "*A method for the production of Brassica oleracea with elevated levels (...) of glucosinolates (...) that include: (a) The crossing of wild species of Brassica oleracea and improved lines; and (b) the breeding of hybrids with a high rate of (...) glucosinolates (...),superior to those initially found in improved lines of Brassica oleracea. [...] An edible Brassica plant produced using the method. [...] 10. Edible part of a broccoli plant produced using the method. [...] 11. Broccoli seeds produced using the method*". However it should be remembered that in its article 53, the European Patent Convention clearly states that "European patents shall not be granted in respect of: (b) plant or animal varieties or essentially biological processes for the production of plants or animals; this provision shall not apply to microbiological processes or the products thereof". Consequently, the Technical Board of Appeal of the European Patent Office has raised a number of questions, such as " if a non-microbiological procedure for plant production that contains plant breeding and cross-breeding bypasses article 53(b) EPC, in particular due to the fact that it contains an additional technical characteristic as an additional stage or as part of any stage of breeding and cross-breeding?". Put more simply, does the fact that it has carried out molecular marking (which can be seen as a microbiological procedure for analysis that facilitates acquisition, but is not an acquisition procedure) allow it to obtain a patent on a conventional plant (obtained through cross-breeding and breeding) despite the ban on patenting biological processes contained in the law? The response of the Grand Board of Appeal of the European Patent Office to this question was that a conventional breeding procedure involving plants or animals cannot be considered an invention, even if it includes an additional technical characteristic.

The Argentinian soy case

The case filed by Monsanto in Europe in 2005 to recover royalties not received[35] in Argentina on its Round-up Ready soy (RR) is another example of the legal battles in relation to the industrial property of cultivated plants. Monsanto sought to recover its royalties from importers of RR soy meal, since they had not been paid by Argentinean producers, Argentina does not recognise patent rights on plants. The decision of the European Court of Justice ruled against the company, recalling that "article 9 of Directive 98/44/CE of the European Parliament and of the Council of 6 July 1998 [...] does not confer protection to patent rights [...] when the patented product is contained in soy meal, where it does not

[35] Furet A., "Affaire des royalties sur le soja argentin: la Cour de justice de l'Union Européene statue contre Monsanto", Inf'OGM, July 2010. http://www.infogm.org/spip.php?article4495

exercise the function for which it is patented".[36] In short, the patent on RR soy meal is on the genetic modification that makes it resistant to RoundUp, concerns the farmer but not the European consumer, for whom this would make no positive difference. Debates/disputes in relation to patents are nowhere near resolved, with the issue being, as we shall see, the industrial protection of plants in the field.
Apparent trends clearly show this. As for Monsanto, the company has pulled out all stops to assert its rights: prosecution of farmers, court cases against Argentina, then in Europe. The Broccoli case also shows that there are strong divergences among agricultural actors themselves. Thus, the association Croplife, which brings together the main biotechnology companies such as Syngenta and Monsanto, hoped for a positive response from the European Patent Office on the patentability of a conventional plant based on the presence of a technical characteristic in the course of its production. For their part, the European Seed Association, the ISF, agricultural trade unions and NGOs have campaigned for a negative response.

Patents and NPVC: Indexing genetic information strengthens the industrial property of seeds

Guy Kastler, Réseau Semences Paysannes

From the beginnings of agriculture to the first green revolutions in the 1950s, it was farmers who bred all the plants we eat. Since then, the seed industry has merely drawn on this immense diversity to develop strains that have been adapted to petrochemicals and replaced 9 out of every 10 farmers with polluting waste from fossil fuels. By limiting the seed market exclusively to varieties that have been standardised and stabilised by industry, the seed catalogue prevents competition from farmers' seeds that have been stored in collections of "plant genetic resources". In 1961, Europe refused to patent seeds and opted for another form of industrial property law, the plant variety right (PVR), to regulate competition between breeders while at the same time legalising biopiracy to their sole advantage: recording the description of the morphological characteristics of a plant, whether newly-bred or already existing in farmers' fields without yet having been recorded, allows a claim to be made for ownership of any seed sold that produces plants with the same characteristics. The "breeder's rights" to freely use a variety protected thus to create another variety, results from this specific element of the NPVC: how is it possible to identify beyond doubt the parents of a plant that is the product of cross-breeding by simple observation of its morphological characteristics?
A NPVC to a variety is delivered on the basis of three specific criteria (DUS), established by the Union for the Protection of New Varieties of Plants (UPOV): varieties must be different from all varieties previously recorded, uniform (made up of identical plants) and stable (the characteristics of the variety are maintained through the first harvest of each batch of seeds sold). Originally, DUS was measured exclusively on phenotypical characteristics. Since the new UPOV convention of 1991 it has related to "characteristics the product of a genotype or combination of genotypes", opening the door to molecular or genetic characterisation. These characteristics do not correspond to farmers' seeds, as the latter are sometimes indistinctive, but above all heterogeneous and unstable, as they are constantly adapting to their environments.

Farm seeds become counterfeit

In 1994, the European Union published regulations for the application of UPOV[37] accords dating back to 1991. These European regulations describe farm seeds as counterfeits and extend the protection of the NPVC to varieties that are "essentially derived" from the protected variety, extending it to the product of the harvest. However, due to resistance from farmers, the proposed ban of farm seeds that farmers save from their fields to resow did not extend to 21 of the most important farm seed varieties. Only one obligation to pay royalties to the breeder was established. However, breeders have encountered great difficulties in recovering royalties on varieties of farm seeds that they have protected, since the variability of plants that evolves with each cycle of reproduction means that they cannot prove at a reasonable cost and beyond doubt, that a plant sown by a farmer is indeed of their variety rather than another one (thus clearly demonstrating the instability of varieties).
The extension of protection provided by the NPVC to the "essentially derived" variety, to which a competitor need only add patented genetic information, allows licence fees to be shared between the owner of the NPVC on the variety and the owner of the patent on the gene: this opens the door to new varieties of GMOs in Europe. Extending the protection to the product of the harvest makes this NPVC a higher performance tool than the patent. Indeed, it does not require the expression of the function of patented genetic information in order to be exercised: in the case of the dispute on Argentinean soy meal cited above, Monsanto could have recovered its royalties from European importers had it protected its varieties containing a patented gene with an NPVC.

In 1998, Europe legalised patents on genes and combinations of genes and their functions (Directive 98/44). Industrial property then became more easily identifiable, using an inexpensive molecular analysis on farm seeds, the contaminated harvest or the competitor's variety. The owner of the NPVC on the variety containing a patented gene can thus claim a sufficient presumption of counterfeit to effectively claim the payment of royalties on farm seeds in the same way as the owner of the patent in the event of the use of "their" genes by a competitor.

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[36] Decision of the Court (Grand Chamber) of 6 July 2010, Official Bulletin of the European Union of 28 August 2010, C 234/7

[37] Union for the Protection of New Varieties of Plants, of which the European Union is a member.

Lack of clarity of property rights

With transgenes subject to compulsory information under the directive on the release of GMOs into the environment (2001/18), plant breeders know if the variety they are using to select another does or does not contain patented genes. This is no longer the case with new patents filed on genes produced by unregulated technologies such as site-directed mutagenesis, or even genes whose function has only been identified. Thus, a variety that is specifically herbicide-tolerant to may be the result of breeding plants cells that have a "natural tolerance" in artificial laboratory conditions, or breeding the tolerant gene of a "natural mutant" found in the field via marker-assisted retro-cross-breeding; these biological breeding procedures cannot in theory be patented in Europe. Chemical mutagenesis, or direct ioniser can produce a variety that is similar from all points of view; this is a patentable microbiological process. It is however impossible to distinguish a plant produced by a first variety from another plant produced by a second variety, using genetic or molecular analysis. Although the first plant is the product of a traditional breeding method, and the second is an unregulated GMO, on which consumers are provided with no information. Moreover, the first plant is only covered by a NPVC (in Europe), and can therefore be freely used to breed another variety. The second is covered by an NPVC and by the patent on the microbiological breeding process, the protection of which extends to all plants to which it confers tolerance to herbicide.

The presence of this tolerance gene that can be identified by genetic or molecular analysis does not constitute sufficient evidence of patent conterfeiting, as it could result from a "natural" mutant process. However, it does constitute sufficient grounds for court actions that more often than not do not lead to actual court cases, but to an "out of court settlement" between the firms in dispute that favours the firm with the greater financial and legal resources, as a settlement always costs much less than endless legal proceedings, even when one is sure of victory in the case of such cases. This surreal situation is possible due to the fact that the only information available when seeds are sold is the name and characteristics of the protected variety indicated when the NPVC is filed with the Community Plant Variety Office (CPVO), which says nothing about the patented genetic combinations contained in the protected variety. Patents filed with the European Patent Office (EPO), on the other hand, do not indicate the varieties in which it is used. The CPVO knows nothing of the presence or otherwise of a patented gene and the EPO knows nothing of the varieties protected by NPVC in which the patent is used. Thus, consumers do not know what they are buying and eat genetically modified plants, while breeders do not know if the resources they use for their breeding are free of licence fees or not. It is not until the end of the process of developing a new variety that they learn whether or not a patent can prevent its sale.

This does not prevent some of the patents from claiming an extension of their rights to the whole food chain. This accumulation of the patent and of the NPVC thus facilitates the sale of these "illegal GMOs" to those who do not want them, impedes industrial innovation, and accelerates the concentration of the industry, which is already exists in the case of transgenic GMOs. This benefits those who hold the largest patent portfolios, most of whom are from the US. It also puts paid to the right of farmers to resow part of the seed that they have saved from their harvest or to breed their own seeds. Indeed, farmers have even fewer resources than breeders for determining the existence of these patented genes and, when they do discover them in their varieties following an "accidental" contamination, they have no technical tool for isolating these genes and extracting them from their seeds: the fear of possible unforeseen legal proceedings will soon dissuade them from resowing part of the seeds harvested or using them to breed their own varieties.

Latest developments to renew the European framework

One of the stated objectives of the evaluation of European legislation on property rights to plants entrusted to consultants GHK by the European Commission on 4 May 2010 in the name of "*cost cutting*" is the harmonisation of national laws in a move towards a single NPVC and a single European patent. Several other avenues for the evolution of these laws are also explored:

- As regards "*genetic resources*", the pharmaceuticals industry is increasing the number of its initiatives to ensure the application of obligations to "*reach a prior agreement on benefit sharing*" (ABS) resulting from the Convention on Biological Diversity in European law, in order to facilitate their access to expertise and to traditional medicinal plants that would enable them to prepare new patented synthetic molecules. As a result, large seed-producing countries (France and Germany) are preparing to incorporate their national collections into the multilateral system of the ITPGRFA[38], which enables the seed industry to sidestep these obligations. This system repeals the prior agreement on access to genetic resources by a State, and exonerates the owner of an NPVC from having to share financial proceeds on the grounds that it is leaving "the resource free for research". The owner of a patent, for their part, is under no obligation to indicate where the genetic resource has been identified. As regards the NPVC, a task force at DG Sanco (Directorate-General for Health and Consumers) is looking into various means of allowing plant breeders to "recover funds lost through farm seed use", i.e. their royalties each time a farmer resows part of their crop. It proposes to involve States in the hunt for counterfeits, in particular by requiring the name of the variety used to be included in the obligations of eco-conditionality, with which all farmers must comply in order to access CAP subsidies, and the market. The European Commission is also proposing to include seeds in the Anti-

[38] International Treaty on Plant Genetic Resources for Food and Agriculture, www.planttreaty.org/index_fr.htm

Counterfeiting Trade Agreement currently under negotiation. Molecular marking to distinguish two different varieties can also be used as additional means to "prove" that a farm seed or imported variety is counterfeit.

- As regards the patent (Directive 98/44), the Dutch government supports the request made by its seed industry to extend the "breeders' rights" to any form of patent that currently limits the use of seeds for research or selection. The French Seed Companies Union has, for its part expressed its concerns in light of the multiplication of unidentifiable patents that protect genetic information contained in seeds. It underlines the risks of a total freeze on innovation by companies with the largest portfolios of patents, a situation that is aggravated when these patents protect "native" genes (those which already exist naturally)[39] and is demanding that breeders' rights be granted. The German government is also preparing an initiative to support the evolution of plant patent law.

Farmers rights in the regulatory battle

Behind the opposition by European industrial seed companies to the "seed patent"- which does not exist in Europe since plant varieties are excluded from this patent - we can witness the bargaining that might take place at farmers' expense taking shape: agreement to limit the extension of protection provided for patents on "native" genes and the exemption of research, on the condition that the possible combination of the NPVC and the patent be retained, and to force farmers to pay royalties on all farm seeds payable under the NPVC. This would also be a way of reinforcing the legalisation on biopiracy. Thus, the debate on the GM or non-GM nature of organisms that are the product of new genetic technologies resembles a new episode of the commercial disputes between various factions of the industry that is now focusing on the limits on patent protection, whereas the problem lies in the very existence of industrial property rights on the living organisms, and not in their limitations. It is a matter of urgency that in this debate, farmers raise:

- The recognition of their rights, as set out in the ITPGRFA, to conserve, use, exchange and sell their farm seeds and protect their knowledge
- The ban on any form of patent on seeds, their genes or the modification of the same using genetic technologies, as well as of the NPVC of 1991, which renders farm seeds counterfeit.

General considerations in relation to the appropriation of living organisms

Industrial property law is evolving in line with techniques, allowing what some denounce as an appropriation of living organisms. This use of the law is confirmed in the trend seen in patents filed between 1980 and 2008, with a fall in the number of patent applications in the area of genetic engineering alone and an increase in the number of patent applications for conventional improvement procedures associated with genetic engineering. With the substantive work currently in progress to ensure that new biotechnology techniques are not considered GMOs, the use of molecular markers in plant improvement procedures that result in a patent being granted, would indicate that companies are simply aiming to obtain industrial property rights to native genes and selection techniques. If this occurs, biotechnology techniques will probably not be further developed unless they allow a plant to be modified and industrial property to be obtained.

Moreover, the intended use of these patents is not always aimed at a commercial application, with a number of patents allowing companies to adopt a standby position, keeping a highly efficient tool to improve competitiveness (to say the least) in reserve. In the medical field, some researchers are mobilising to denounce their inability to conduct their research as a result of patents on genes involved in diseases, which in a different way illustrates that patents hinder research rather than promote it.

While industrial property law in itself is not new, the growing concentration of the seed sector in the hands of chemicals companies as part of an approach driven more by financial considerations than productive ones certainly is.

This economic phenomenon changes the parameters of the problem, since these companies are far removed from the world of agriculture, and somewhere along the way their policies seem to have drifted away from taking the working conditions in the farming sector into account. Moreover, we have seen that while modes if industrial property differ according to company strategies - NPVC for seed companies producing new varieties, and patents for chemicals companies that produce genetic modifications – the combination of these two systems is liable to result in the almost complete appropriation of living organisms and plant genetic resources.

[39] Cases brought in Munich against patents on broccoli shoots and wrinkled tomato had to respond to this question of extending the protection of an invention that consists of "determining the genes that give rise to a particular property" to the protection of "production" of this property within a plant via natural procedures (traditional marker-assisted breeding).

3. Epistemological and ethical issues

In this third section, we have sought to consider the reasons for this persistent move towards a greater artificialisation of living organisms. Of the eight techniques under discussion at European level, one has not been developed in the first section of this brochure: synthetic biology. We have decided to address it here with the epistemological and ethical questioning of new techniques for the modification of living organisms, as it prolongs and systematises the orientations of other techniques, proposing to create a totally synthetic, non-natural organism. In his first intervention, B. Eddé in the first speech explains its principles and raises the epistemological positions of researchers involved. While the synthetic living organism is the end product of the evolution of techniques in which biological engineering sciences come together, it is also the product of a vision of the world. The limitations of techniques are presented in greater detail and within a broader framework in a second speech by F. Jaquemart, who raises the in-depth social debate on the headlong rush to growth in a finite world. In a third speech, S. Pouteau critically analyses the scientific method. She states that we have all of the elements needed to avoid treating living systems like a Lego set, which raises question of the approach to developing these techniques, the values implied, and the world in which we want to live.

The principles of synthetic biology

Bernard Eddé, BEDE

Synthetic biology has flourished since the early 2000s; it is noted for original avenues of research and technologies, and particular epistemological and philosophical positions. The term resurfaced in the late 1990s to refer to a set of approaches that aim to design, construct (two major terms) or modify (minor term) living organisms that possess properties that are not found in nature. Nowadays it is a recognised discipline involving several hundred companies and thousands of laboratories.

Today, more than 18 European programmes are contributing to this work and, as a result, it benefits from considerable public and private investment. Its stated objectives are both cognitive (it is by reconstructing life that one can understand it) and aimed at highly ambitious applications: "To satisfy the unlimited needs of man within the context of limited resources" (Endy, 2005). Synthetic biology is a typical example of techno-science, where there are close ties between scientific discoveries and technical applications to the point that they become one. There is no more time for reflection on and analysis of a scientific innovation, as it is immediately taken over in the economic sphere to develop techniques that have industrial applications.

The different avenues of research in current programmes

There are four main avenues of research: the constitution of a bank of "bio-bricks" - proto-cells - minimal cells - and the engineering of intercellular communications.

Bio-bricks

These are collections of DNA segments, copied/pasted from natural DNA sequences, or via direct chemical synthesis, that encode biological data of "elementary components": proteins or protein domains (enzymes, binding domains, interactive proteins, etc.), promoters, terminators, cloning and recombination sites, etc. The objective is to provide the base elements for assembling functional systems.[40] Once inserted in the appropriate vectors, these DNA constructs can be introduced into host organisms either via traditional transfection techniques or as much more ambitious projects, such as synthetic genomes (see below).

What is the difference between this and traditional genetic engineering? For scientists in this area of research, the issue is precisely to avoid the inherent limitations on the effectiveness of these techniques. Bear in mind that more complex functions involve a number of genes. For example, the biological synthesis of artemisinine, a therapeutic compound used to treat malaria, requires 11 different genes to be introduced into bacteria or yeast. The resulting complexity cannot be controlled using traditional techniques. For new synthesisers of living organisms, the control provided by engineering sciences and modelling methods would facilitate a specific description and prediction of how this system operates. Moreover, interfaces are standardised (restriction sites) to allow bio-bricks to combine at will (in 2008, the collection contained some 3,200 elements, all combinable with each other). In short, the approach is gradually moving towards an increase in synthetics, inasmuch as DNA sequences are no longer obtained by copying existing genomes but rather are devised by their designers and chemically synthesised using increasingly effective DNA synthesising equipment. In terms of application, enzymes that cut DNA, such as zinc finger nucleases, are a product of this approach (see figure on page 12).

By using the standardised elements of the bio-brick collection, synthetic biologists can already, to a point, programme living systems in the same way a computer scientists programmes a computer.[41]

The two key words in these works are *rationality* and *machine*, since they determine the approach adopted by the researcher.

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[40] In general, these systems contain one or more active elements (encoding DNA sequences for enzymes, scaffolding proteins, transcription factors, etc.) and regulating elements (sequences that regulate DNA) that modulate the expression of agents according to complex schemas: oscillations, amplifications, feedback, etc.

[41] http://biobricks.org/

Synthetic cells (proto-cells)

This is an approach firmly rooted in an older tradition of research into the conditions for the emergence of life. Its ultimate aim is to build living systems in a completely artificial manner, in the form of self-reproducing machines. The first phase consists of developing artificial encapsulation systems, such as lipid vesicles that form a semi-permeable border with the environment ("proto-cells"). The synthetic devices inserted in these vesicles must then ensure all general survival and auto-reproductive functions, as well as specialist functions required in view of their applications. However, this avenue of research is still in its infancy and possible applications appear somewhat far off.

Minimal cells

At first glance, this avenue of research appears closer. It anticipates the fact that the obstacles encountered by traditional genetic engineering will emerge again with bio-bricks, due to the interference of recipient organisms. Existing organisms have been fashioned by evolution over billions of years; as a result, they represent a certain "engineering logic" of nature and are, at the same time, the product of particular historical contingencies. Eliminating what is contingent in order to preserve only what is essential to their survival and reproduction would therefore, according to this approach, reduce their complexity and minimise the interference they could produce on the functioning of systems inserted.

Thus, the specific aim is to replace the genomes of existing organisms with simplified genomes, obtained via the chemical synthesis of DNA. Organisms thus modified would be used as "cell frames" into which required combinations of systems could be inserted on demand, with a view to intended applications.

Work done in this area to date has shown that 15% of genes of the E. Coli bacterium could be eliminated by modifying the genome. With the constant improvement in the performance of equipment, the direct synthesis of DNA has become the predominant technique. It has allowed the synthesis first of small viral DNA (X174, polio), then of the genome of a bacterium (DNA of 500,000 bases). Finally, in May 2010, J.G. Venter and his laboratory announced the complete synthesis of the genome of the mycoplasma mycoides bacterium (a million bases) and its transplant into a related species. According to the authors, this experience is but an initial stage that aims to provide "evidence of the concept": an entire genome can be artificially produced and replace the natural genome of a bacterium. The bacterium "created" thus[42] is viable, can proliferate and has at least some properties of the donor bacterium.

Therefore, according to the authors, one could create organisms capable of performing tasks as diverse as producing biofuels, decontaminating the environment on demand, or even synthesizing medicines and functional food... Will these promises be kept? Will organisms obtained thus be viable in the long-term? The experience described does not provide an answer to these questions. The synthesised genome is an almost a perfect copy of a natural genome, with various micro-organisms used in its "production", which puts the creative nature of the experience and its basis in the “synthetic” into sharp relief. Moreover, the analysis of the properties of man-made bacteria is far from exhaustive. The main role historically given to the genome is disputed, and other less controllable factors, in particular epigenetic factors, can come into play. In short, it remains to be seen that experience of the microorganism in fact constitutes "proof of the concept", that it can be generalised to apply to other organisms (with walls, as in the case of plant cells), that the complexity of the genome can in fact be reduced and that artificial devices can be introduced there and function in a predictable, reliable manner.

The engineering of communications between cells

With this type of approach, we start to see a greater influence of systematic thought and the biology of systems. the approach that guides them is to consider that biological devices, whether natural or man-made, are not intrinsically accurate and reliable, but make a lot of noise and are random. Rather than seek to render them reliable by eliminating the random element of their operation, the idea is to come up with a superior biological approach for populations. The way an organism operates is no longer considered independent of its interactions with individuals of the same species, let alone those with different species.

Let’s take the example of artemisinine: rather than inserted the 11 genes involved in a single individual to be multiplied to infinity, this approach could favour the use of several populations that each receives a subset of genes. The intermediate products secreted by a population would then be metabolised by others in a system where different populations cooperate to produce the desired compound.

Thus, the objective is no longer to modify a given organism in depth, which, according to the authors, cannot lead to reliable functioning, but rather to design "synthetic ecosystems" oriented, thanks to the genetic modification of different populations or species, towards the production of the function sought.

Epistemological and philosophical positions

From the outset, researchers in synthetic biology have declared their ambition to "create" new life forms. On an epistemological level, there are two characteristics. The first can be illustrated in a quote by physicist Richard Feynman ("What I cannot create, I do not understand") often cited by synthetic biologists, who thus call into question the relative separation, even though it has already been undermined in part, between knowledge initiatives and applications. In synthetic biology, both approaches are thus closely linked and lie fully within the techno-science paradigm.

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[42] The title of the article, which was published in the magazine Science in July 2010 (vol 329, pp 52-56), refers to the ambition to "create": "The creation of a bacterium cell controlled by a chemically synthesised genome".

The second characteristic concerns the role played by the concepts and methods that arise from engineering in knowledge of living organisms. The aim is no longer to obey the natural processes that give rise to living beings, which by necessity are imperfect due to historical contingencies linked to evolution, but to rationalise them, and translate them into simple engineering principles, to think of them as an arrangement of detached pieces conceived from scratch, rather than as whole entities. This is the engineering approach vs. the approach of nature.
These epistemological positions reflect more or less explicit philosophical standpoints. What does it mean for human beings to create living beings, to push the artificialisation of beings and of nature to the extreme? How will this affect the foundations of our relationship with others, and with the world? How will it affect our conceptions of living systems and of the inanimate?

An analysis of genetically-modified organisms for social change

Frédéric Jacquemart, GIET

"*In my opinion, it is imperative that in our Western modernity we consider new ethics for technology, in order to review our relationship with technical objects to be other than something based on power and consumption*".
Marie-Hélène Parizeau

Reclaiming the fullness of language

"*When the wise man points at the Moon, the fool looks at his finger*", goes the old Chinese proverb. Indeed, the fools are not the only ones concerned; this way of seeing things is widespread. If something moves, we talk about that thing and not about the context, both past and present that has made that thing appear and have a meaning.
When it comes to GMOs, this principle is even recorded in the law: GMOs are evaluated on a case-by-case basis, since each case is different. In view of our high intelligence, we are able to take particular characteristics into account. Except that by doing so, we validate *de facto* everything that is general and philosophically previous, without analysing it. Here, the expression "philosophically previous" means, for example, the decision that being able to do something is enough to justify doing it. Thus, for GMOs, no other justification has ever been discussed by the bodies concerned.[43] We have the know-how, so we create them, and observe to see what happens (without really knowing what we are looking for…).
The new techniques described in this fascicle are just the most recent developments in a bid to dominate and control nature that dates back to the very beginnings of science. Scientific ideology has barely changed since the 17th century, when Descartes declared his intention to "become the master and possessor of nature",[44] or when Sir Francis Bacon declared, in the New Organon that, "first of all, the science we now possess is not for inventing arguments, but arts... and different intentions produce different results: the aim here is to conquer and enslave the adversary by working to this end (in this case, Nature)".[45] The main problem with current technical developments lies in the way we relate to living things and nature in general. It is for this reason that rather than fixate on the problems posed by each of these new techniques, we prefer to attempt to situate them in the vast context of the relationship with living organisms and nature.
On a societal level, one of the most serious, anti-democratic acts with the most serious consequences in the history of modern techno-science has been to deprive citizens of the right to express their opinion and imposing techno-scientific language as the only possible choice, thereby hiding the very nature of the problem at stake.

"Science-based", "Sound science": these are the sorts of expressions experts and political decision-makers revel in, repeating them as though they were psalms quoted by "scientists". It is not just this attitude, which is scientific in the extreme, confines people to blind sectarian belief;[46] but it's a pure incantation divorced from reality, with a failure to observe the minimum level and basic rules of scientific reasoning even in the authorisation submissions for GMOs.[47]

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[43] A distinction must be drawn between motivation (I want to do something) and justification (I have the right to do something). The latter refers to ethics, in which the WTO has declared that it could not formulate an acceptable argument in the evaluation of GMOs...
[44] Descartes, "Discourse on the Method ". The phrase that follows this classic quote is also extremely significant: " This is a result to be desired, not only in order to the invention of an infinity of arts, by which we might be enabled to enjoy without any trouble the fruits of the earth, and all its comforts, but also and especially for the preservation of health, which is without doubt, of all the blessings of this life, the first and fundamental one".
[45] Here, the term "arts" refers to "techniques". On the birth of science and its close relationship with alchemy and religion, one can refer to the volumes of Nissim Amzallag: La réforme du vrai, Ed. Charles Léopold Mayer, 2010, and La raison malmenée - de l'origine des idées reçues en biologie, CNRS Editions, 2002.
[46] For more information on scientism as a modern religion, read "Lettre ouverte aux scientistes" by Matthieu Calame (Ed. Charles Léopold Mayer) and texts by the same author on the GIET website: http://www.giet-info.org/file/Fonction%20sociale%20et%20politique%20des%20savoirs.pdf and http://www.giet-info.org/file/Les-chercheurs.pdf. Two other publications clarify this problem with current democracy: Technology and science as an ideology, by Jurgen Habermas, (Gallimard) and Biotechnologie, nanotechnologie, écologie. Entre science et idéologie, by Marie-Hélène Parizeau (Quae).
[47] According to a recent ANSES report, the minimum requirements for the admissibility of statistical tests are not met in

Nevertheless, citizens are forced to use only techno-scientific arguments, although this is not the fundamental issue at stake, even though this aspect should be treated seriously. This obligation comes from the WTO, the European Commission and national bodies, but also simply from culture, which imposes on each person scope for the acceptability of arguments.
Can we believe that people get arrested of their own free will, appear in court and, in most cases, have rulings handed down against them because there is a gene that provides resistance to antibiotics in a given GMP? This demonstrates the power of cultural inhibition: the very people in revolt stop themselves from expressing what really motivates them: the oppression of scientific ideology emanates from the dominant global paradigm. The return to democracy involves reclaiming language in its fullest expression.

Modernity as a context

Modernity is characterised by one major fact that requires a profound change in ethics: human activity (and therefore, technoscience) has achieved such a degree of efficiency in its interaction with nature that alterations in the latter are becoming significant. It would appear that for the first time in human history, human beings are no more by law to the world[48] and that, as a result, its actions must be now validated from the perspective of the continued existence of the human race in a natural world that can still accommodate it, a continued existence that is no longer *a priori*, as was once implicitly the case.
Already, we can see how useless it is to carry out a case-by-case analysis of GMOs, since by proceeding in this manner one places oneself *de facto* in the traditional ethical context, which, while part of our cultural inheritance, is both obsolete and questionable. The evaluation of GMOs and, beyond this, the evaluation of technologies in general as currently occurs, is missing the most essential point.
Nature is comprised of elements - living and non-living - connected to each other to form an extremely complex dynamic network of interactions. Philosopher Michel Serre[49] called such a system "biogea". Like any network for interaction, this biogea has an organisational form[50] that depends on constituents and modes of connection between them, with the constituents and connections themselves dependent on the organisation of the system, a circular structure typical of self-organised systems. This organisation in itself is constantly evolving, and we have found that to date its spontaneous nature is compatible with the existence of humans. Tinkering with this organisation may cause it to be no longer compatible with our existence as a species, or our existence could be rendered much more difficult than it currently is. Again, it is this situation, where our presence in the world as a species is clearly becoming dependent on our actions that characterises the modern age and requires a radical cultural change in order to adapt to this modernity.
It is impossible to infer global behaviour of a complex system based on local data. One of the main issues is to find out if impossibility is caused by the system itself, or is merely a de facto one, with the latter hypothesis leaving open the possibility, in the future, of making this type of prediction. At any rate, it is currently not possible to make such a prediction[51] of the effects of our actions on the organisation of the biogea using scientific analysis.
And yet, the issue, which, again, is nothing less than our own survival as a species, requires us to carry out an evaluation of the GLOBAL effect of new technologies, or at least of recent ones. We will not cease to act, or even to innovate, but we can no longer do so with our eyes shut. This need for a change in the issue of the evaluation of actions has begun to emerge in the public awareness. This is illustrated in a paragraph from a tender launched by the French government in 2011:[52]
"*Standard models for the evaluation of health and environmental risks focus on predictable consequences and, more often, on measurable and probable impacts. Rradical uncertainty and indirect consequences are, to a large extent, excluded. Such dimensions are however essential in complex natural and socio-technical systems. It could be appropriate to engage in in-depth analysis of risk-evaluation. [...] In order to predict which response could result from a given action, one could, for example, replace that (vis-à-vis a complex natural system taken as such to determine the "level of organisation") with which there is interference, without attempting to anticipate the form of responses resulting from said interference*".
Thus, the objective is no longer to determine the consequences of an action, but to evaluate the seriousness of said action on the organisation of the biogea, without seeking to predict how the disrupted system will express itself.[53]

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the dossiers, and yet have been validated by European bodies (AESA). The toxicology evaluation is reduced to almost zero, while the allergenicity evaluation would be laughable if the subject were not so serious. In the case of the latter, expertise is said to be based on "the weight of evidence" (sic). In other words, there are no data to support the conclusion.

48 Jonas, H., Le principe responsabilité - une éthique pour la civilisation technologique, Ed. Du Cerf, 1990.

49 Serres M., Biogea, Éditions Dialogues, 2010.

50 The area of organisation is to be taken here in its everyday sense. One can prefer the structural or dynamic variety.

51 This is due to the fact that these complex natural systems are characterised by the existence of emerging phenomena that have no logical connection to what has caused them. Elements for reflection on this issue can be found in the R. Prost film "2+2=bleu" (http://giet-info.org/articles.php?lng=fr&pg=117)

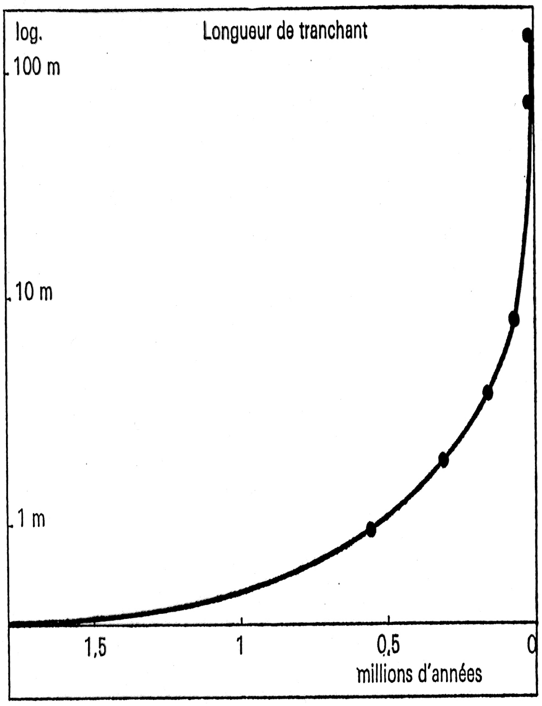
52 The RiskOGM tender, the aim of which was to provide the State with elements that allow decisions to be made in relation to GMOs. The tender received a response from GIET and the ITUS team from INSA in Lyon, along with PEUV.

53 Irrespective of the result of this tender, an approach to this issue will be set out in an upcoming booklet to be

Repositioning ourselves in the general evolution of techniques

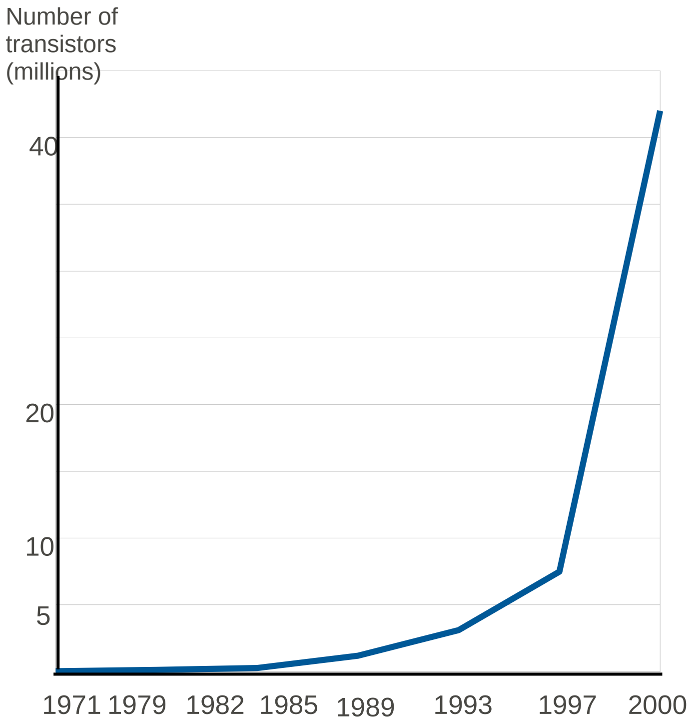
After his work on the evolution of species, visionary philosopher François Meyer (1912-2004)[54] shifted his focus onto the evolution of the sciences and technology. He showed that such evolution was not linear and gradual, as is often believed, but rather resembles an exponential curve: after a long period in which it is virtually unchanged, the curve can rise sharply in an almost vertical manner towards an unreachable infinity.

Length of edge of flint



According to works of André Leroi-Gourhan.

Evolution of power of microprocessors



Graph formulated according to characteristics of Intel processors, available on the entry for 'Microprocessor' in Wikipedia.

Whether it be due to the power available, the number of publications, the rate of renewal of objects produced by technology or other factors, the current explosion of techno-scientific knowledge and know-how is clear.

The invention of plastics, for example, has provided a boost to other techno-sciences, including biology. Working with microplates rather than with glass tubes and benefiting from the ability to fix molecules using polystyrene have led to a considerable acceleration in the development of microbiology, immunology, genetic engineering, etc. Directly or indirectly, these developments foster development in other areas and limit the technical obstacles to this evolution.[55] Inter-potentialisation and the removal of technical obstacles account for an evolution of the type we now see: the greater the level of development, the stronger the potentialisation. After a start-up period for the system, it explodes.

While we are unable to analyse this phenomenon here,[56] it would nevertheless be appropriate to draw out a number of essential aspects in relation to how we look at new techniques for the modification of living organisms:

1) The technological explosion has resulted in an unprecedented capacity to act on nature, resulting in the destruction

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published by PEUV in this collection.

[54] Meyer F., L'accélération évolutive, Librairie des sciences et des arts, Paris, 1947; Problématique de l'évolution, PUF, Paris, 1954; La surchauffe de la croissance, Essai sur la dynamique de l'évolution, Collection Ecologie, Fayard, Paris, 1974.

[55] The transformation of the cultural brake on innovation into the development of innovation, on the other hand, has removed a factor of control that prevented the technological explosion.

[56] On this subject, see the intervention of Frédéric Jacquemart at the "Statut de la science dans la société contemporaine" symposium held on 30-31 August 2008, http://www.giet-info.org/articles.php?lng=fr&pg=90.

of which we are aware. Considering the general speed of progress in techno-sciences, it would appear that this power, sought by Descartes and Bacon (see above) is totally different in quantitative terms to that available in the 17th century, or even the 19th century. The quantitative difference is such that in qualitative terms, it is altogether different, a new situation: catching a tonne of something is not the the same but just heavier than catching a gram of something : in qualitative terms, it is something altogether different. This new situation, never before seen in human history, requires new ethics, a new way for people to relate to the world, and to this break with the past;

2) One cannot carry one to infinity in a finite world. It is curious that scientists do not appear to be able to understand this evidence. This means that, at our current point in this techno-scientific evolution, that this self-amplified process will stop, whether we like it or not.[57] And a fact all too often overlooked by politicians, among others, is that society evolves alongside technology. The evolution of society incorporates the possibilities offered by technological development, and becomes dependent upon them. The automobile does not reproduce on its own; it does not pollinate. Technically, we know how to stop it. And yet, even if there were a veritable will to do so, due, for example, to its harmful effects on the biogea, no one could voluntarily make such a decision. The pursuit of technological growth increases the dependence of societies, and results in ever increasing fragility in the face of change… and this at a time when it appears that this profound change will occur, whether we like it or not, whether we assist it or not.

Yet it is this growth that is cited as a justification *a priori* for all research, and which also justifies *a priori* the sacrosanct "freedom of research ", pursuing objectives from the 17th century but in a historical context that has become incompatible with such positions. Greater knowledge in itself can no longer justify a given action. Modernity requires another opinion and further analysis, in another context, with this analysis to involve civil society.

Necessarily restraint

The biogea, as well as all of the beings that inhabit it, is organised. It is an obvious fact, but no one pays enough attention to obvious facts. What matters to us now is whether or not our actions jeopardise the organisation of the biogea. If so, the precautionary principle is justified, and there is no need (nor is it possible) to describe the events whereby these organisational changes would have manifested themselves. Thus, it would be appropriate to see what determines the possibility of being organised.

The main characteristic of an organisation, which we shall say is the product of chance, is that it is different from chance.[58] Essentially, what is organised is opposed to "random occurrence". If everything and anything is possible, there is no organisation. Therefore, organisation will be what puts paid to the totally random range of possibilities.[59]

For example, even if the current state of an object that is organised (one possible arrangement of the atoms that comprise it) is just as likely to be the product of any other arrangement of these same atoms, and which itself is the product of random occurrence, in our opinion it is impossible for this state to be the “direct” result of a lottery selection. Through this “direction”, it is clear that in essence, the resolution of the paradox implies a need to draw on the notion of historicity.

If, to the eye of the observer, it is clearly impossible for a random process to produce an organised being (equivalent to a lottery drawn from all possible states), it implies that what is organised for us is extremely rare in relation to all possible states.[60] Thus, the probability of making an error when confirming the non-random nature of what appear to us to be organised, is infinitely low (but knowledge is a gamble). Thus, what is organised must necessarily represent (in the philosophical sense of the word) a very small category of realisable outcomes, but a category of distinct elements. The unorganised appears to us to be an immense category of equivalent elements.

Unless the world we contemplate is no more than an illusion, we have come to the conclusion that the real world supports our notion of organisation and that, therefore, another major condition for the emergence of an organisation (and form) is the major restraint on what it is possible to achieve, which is an historical restraint in itself.

It is clear that transgenesis transgresses two fundamental organisational principles. Taking a genetic sequence that has an evolutionary path, to artificially (intentionally) introduce it into an entity with a different history is tantamount to denying *de facto* the relevance of historicity in the organisation of systems, without raising the issue itself. The principle of restraint has also been breached. All genetic exchanges are restricted. In our opinion, although a very large number of genetic exchanges occur, they do not happen in a random manner. Sexual relations are obviously very restricted (hence the rather hollow idea of the "species barrier"[61]), but viruses also have very strong constraints in terms of molecular adaptation, as do bacteria "pili".[62] Even the transfer of DNA created in bacteria is not totally random.

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[57] Hence the need for a change in the global paradigm, a veritable cultural metamorphosis, cf. http://metamorphose-culturelle.org.

[58] This apparent paradox has not been seen for a long time; nevertheless, it would be advisable to specify the state of chance, i.e. its relationship with the observer.

[59] Jacquemart F., Préliminaires à une théorie générale anthropocentriste des objets mous. Scientific thesis, Paris VI.

[60] A formal demonstration was provided by F. Jacquemart, *op. cit*. A simplified version can be found at: http://www.giet-info.org/articles.php?lng=fr&pg=120

[61] Clearly, the restraints do not need to observe the categories created by scientists. What is important is the extent of any restraints, not the category.

[62] A type of tube that allow bacteria to exchange genetic material.

With regards to synthetic biology, not only is it a clear part of this rush towards infinity described above, but it also aims to produce "components and systems that do not exist in nature".[63]
With regards to the creation of new DNA bases, which have never existed, it is said that this has the advantage of preventing the dissemination of organisms thus created, which cannot survive without technical assistance. This can be valid as part of a traditional evaluation of local causalities, but compared to a global evaluation the transgression is even greater than in the case of transgenesis.
Another (global) approach is possible and necessary. Time should be taken to develop it sufficiently before rushing headlong into developments, blinded to our own capacity to exist.

What epistemological questions arise?

Sylvie Pouteau, INRA

From GMOs to synthetic biology, the same desire for control is expressed against what constitutes the most fundamental properties of life: freedom, autonomy, the ability to set our own rules and to contravene them through creativity, inventiveness, and the proliferation of the diverse and the colourful.

And you will be like Cartesian gods

If we wonder about the meaning and rationality of technical evolution, we should bear in mind that scientific enterprise is more about the exploration of the possible than a philosophy of knowledge.
Facts are not made up... until after they have occurred, i.e. created through experimentation: fundamentally, the world is concocted in the retort, as in the age of the alchemists; biotechnologies are the obvious illustration of this. With these techniques, the imagination overlaps with reality: far from having been overwhelmed by the *Enlightened*, imagination has retained all of its vitality and prolificacy. Thus, GMOs that are possible, or probable, with a few makeshift repairs here and there would already have become “MMOs": man-made organisms. Yet to date, there is nothing to suggest that this imaginary vision will never come to fruition; only the proof of experimentation will provide the answer to this question. But we are right to pose the question: what metaphysical exercise are we undertaking? What is our imaginary world?

As explained above, the most spectacular developments in new technologies are due to synthetic biology; this discipline is radicalising the Promethean approach of biotechnologies. That said, little has in fact changed since René Descartes in terms of substance. It must not be forgotten that, in the imaginary Cartesian world, the model of the god who produces living machines is Man himself. "*I assume their body to be but a statue, an earthen machine formed intentionally by God to be as much as possible like us. Thus, not only does He give it externally the shapes and colours of all the parts of our bodies; He also places inside it all the pieces required to make it walk, eat, breathe, and initiate whichever of our functions can be imagined to precede from mere matter and to depend entirely on the arrangement of our organs*".[64]

With God having departed the science scene (at least have seemed to), the (human) model is now free to take over the manufacture of living organisms, or at least to imagine it. With synthetic biology, utopia seems within reach. We are no longer dealing with the springs and pulleys mentioned in Descartes’ works, but "bio-bricks", protocells, and minimal cells. While the composition may have changed, the aim is still to produce living robots from basic elements. With synthetic biology, the world of the cyborg has opened wide before us. We already knew how to compensate for deficient biological functions with artefacts (drips, pacemakers, artificial stomachs, stents, etc.). Now, we can invent new molecular assemblages and new functions, such as meganucleases and zinc finger nucleases. Consideration is also being given to introducing biological devices into instruments to make them more sensitive, retroactive, etc. In reality, if we adhere to the definition provided at the start by Clynes and Nathan Kline[65], we will see that the life of the cyborg began long ago, with the beginning of technology: flints, the plough, the telescope, the mobile phone. We craft, we produce, we create, to use the words of Gilles Deleuze and Félix Guattari. But what is it we are machining?

Technology according to model: An externalisation of our organic impulses

Can we manufacture life after all?
Only the hypothesis of a genetic programme can entertain the illusion that by merely introducing a synthesised genome into an existing bacterium can a living cell be “created”.[66] On the contrary: far from demonstrating that living organisms are the product of genetic determinism, does synthetic biology not demonstrate that what cannot be produced, at least

[63] http://www.synbiosafe.eu/index.php?page=synbiology
[64] Descartes R. (1662), Treatise of Man, translated into French in 1664, cited in Canguilhem G. (1965) La connaissance de la vie, Vrin, Paris, (published in 2009), p. 143.
[65] To refer to the external extension of an organisation complex, functioning as an unthinking integrated system, we propose the term "cyborg" cited in Hacking, I. (2007) Canguilhem parmi les cyborgs. In Braunstein J.F., Canguilhem. Histoire des sciences et politique du vivant, PUF, Paris, p. 125 (the original article by Clynes, M. and Kline, N. ("Cyborg and space") appeared in Astronautics magazine in 1960).
[66] Gibson D.G. et al., "Creation of a bacterial cell controlled by a chemically synthesized genome", Science, 329, 2010, pp. 52-56 (publications by the Craig Venter Institute).

for the moment, is the cell? As regards “artificial intelligence", the question has been posed as to what can be simulated and reproduced by a machine is in fact intelligence. Fundamentally, the intuitive provisions of ordinary life – which enable us in particular to capitalise on sensory and motor perceptions at the same time – are a manifestation of higher intelligence that exceed the capabilities of the most sophisticated machines. Similarly, one could ask whether or not what can be synthesised is indeed "life", or simply a material support for life.

In reality, the possibilities explored by synthetic biology remain for the most part modelled on living systems: the synthesis of known genomes, the use of existing cellular "receptacles". To do this, not only is chemistry required, but biochemistry as well: without enzymes and without cytoplasms extracted from existing organisms, nothing is possible. Thus, life remains a precondition for life itself. Finally, from Descartes to synthetic biology, the model of the living organism is the living organism. The explanation, which can also be found in André Leroi Gourhan (*Gesture and Speech*) and whose origins can be traced back to Henri Bergson (*Creative Evolution*), is clearly translated by Georges Canguilhem (*Knowledge of Life*): it is that of a logical and chronological anteriority of the organic over the technical, and of the technical over science. Technical action is a result of organic activity and not the product of knowledge; it is always tentative before it is mastery of knowledge. It is for this reason that living organism are still the model for the machine and not vice versa, even if countless "bends" appear between the hand and the space rocket.

A philosophy of conditioning: The destruction of sense

If it is impossible to manufacture life, why speak of "artificialisation", whether to praise it or condemn it?

Engineering methods only systematise the suitability of the living organism for learning via the exploration of possibilities. However, exploring possibilities is to make these worlds a reality, to enhance these worlds; finally, it is to establish them as norms. The reference to Canguilhem is again appropriate: the norm is not an average, much less a universal and necessary law: the norm is always the result of a choice made by an autonomous subjectivity, that of a living being, in the experience of its local and historic singularity and in its "debate with its environment ". Accepting and enhancing the decisive action of the environment or the genome is to deny the vital origin of any norm and to authorise the unlimited exploitation of living organisms by living organisms, of man by man. Naturally, the living system can only rise up and resist what has been described as a totalitarian doctrine of conditioning and modification. The artificialisation that has been denounced is not the "production" of living organisms but their conditioning, a conditioning that is arbitrarily imposed from without, and without its involvement. This is not the production of possible outcomes that is impossible, but a prohibition to develop, devalue, create sense and value through debate amongst ourselves, and with others.

The tech bubble: One last acceleration before the end of an era?

Does synthetic biology constitute a mutation in biology or is it simply one more phase in a rational path that is already being implemented through molecular genetics?

For some, the adoption of an engineering rationality would introduce a paradigm shift. But is this shift technical (power, control), scientific (knowledge, explanation), moral (intentionality, transgression), or even logical (internal contradiction)? As mentioned by Frédéric Jacquemart (see above), the works of François Meyer show that major technical developments seem to obey the same rule of self-amplification, which at the same time contain the seeds of their own destruction. Each time technological development enters a period of excessively exponential acceleration, a shift occurs: the technique is no longer used, as it is for something entirely different, with no continuity with what came before it. Thus, technological overdevelopment would appear to be inevitable, as would the paradigm shift, with evolution after the shift impossible to predict. Continuing the analysis of Meyer, Frédéric Jacquemart supports the idea that when all indicators are taken into account, technological development as a whole is now in the final phase of its ascent, and that we are therefore on the verge of a shift without precedent since the Neolithic period.

Despite what is considered "modern" thinking, we are still living in the *Common Human Pattern*, i.e. a new way of life and of relating to the world which has been present since the Neolithic revolution, and which was marked by the emergence of agriculture.[67] In terms of evolution, the Common Human Pattern spans just 4% of human history. But within this new way of life, everything has happened as though each thing had found a natural place, as if nature and human existence had always been thus: nature now has an agricultural outlook and the savage state bears the footprint of fire, the plough, and seeds. Since the Neolithic period, the domestication of plants, agriculture and food have continuously been at the heart of our primordial preoccupations and our imagination. Today, the food crisis combined with the energy crisis can be more deeply expressed as the crisis of the *Common Human Pattern*: suffice it to say that the shock could be phenomenal.

For 10,000 years, we have tamed plants by "growing" them. In reality, however, it is plants that have made us subservient to them, "cultivating" us and rendering us dependent on them for all of their services (in particular food and energy). For some people the is only a single form of logic involved from domestication to GMPs,: that of an ever-improving use of these services. While GMPs are an integral part of the global crisis of technological overdevelopment,

[67] Zwart H., "Biotechnology and naturalness in the genomic era: Plotting a timetable for the biotechnology debate", Journal of Agricultural and Environmental Ethics, 22, 2009, pp. 505-529.

it goes without saying that it is not this or that molecular rearrangement that matters, but rather the total path of domestication. Can GMPs and new techniques serve as tools to analyse where we are in this regard, where we are going, the nature of our relationship with the world, the world in which we wish to live? And if GMPs were just one of several factors in the crisis of the Common Human Pattern: do plants not exist to push us "beyond" and anticipate the inexorable shift? To overcome the barbarism of animal survival instincts, is the peaceful plant not an inspiration to encourage us to return to its ontology and question our "presence in the world"?

The end of biology or the beginning?

It could be said that biology has successfully fulfilled its aim of becoming an integrated discipline. Gone are the dark days of fluids and humours, of animal spirits and kingdoms separated by invisible barriers. Thanks to cell theory, we now know that all living organisms are built according to the same model. Moreover, with genetic programming theory, we even have the assembly plan. Our landscape has broadened considerably: all along the horizon, we can now see splendid cellular monuments and molecular fields that flutter in the breeze. Thanks to biology, the flower can finally be seen "separate from any bouquet", to quote an expression used many times by Stéphane Mallarmé. Biology has also succeeded in its efforts at unification, we can even ask what now sets it apart from physics. Disaggregated life in a corner no longer allows what distinguishes it from non-life to be perceived. In fact, molecules are never anything other than molecules. With correct use and a good toolbox, any engineer or physicist should be able to build their own living machines. Will biology, despite its best efforts, end up as no more than an annex to physics?

The analysis would conclude that it is impossible to say what life is.[68] Having dissected everything and found no trace of an essence, no fountain of life, researchers must proceed with caution. In the end, life will be no more than a nominal definition, i.e. a word – words must be found for everyday language. Synthetic, the term that sums up biology: life will never be more be more than a construction of the imagination. One detail in this beautiful approach, however, has not yet been understood. For each and every human being, there is nothing nominal about being alive or not alive. Never has there been such a fear of death as there is in our time: reversing inevitable decline, and hiding the visible signs of this decline, continues to be the great challenge of science and medicine. Thus, faced with the dissolution of life on a physio-chemical continuum, we can make biology and annex to physics or the opposite: in the end, will it not be physics that will be an annex to biology? Life, which cannot be assigned to a locus, will be reign over everything in existence. Imagination for imagination's sake, the thesis of all living creatures has the merit of taking into account the simple fact that everything has a history and that nothing is reversible: this is what provide us with meaning.

General considerations in relation to epistemological and ethical issues

Finally, what is genetics if not the place for debate on living organisms between living organisms?

How to move past outdated instructional models: those of genetic theory, of the organisation of the production of knowledge, of the governance of innovation? The public issue of GMPs, now new techniques and synthetic biology, are not the product solely of science, which has all the elements required to conclude that the living system is not a Lego set. Nowadays, it is not about a particular discipline (philosophy), but rather about individual ethics founded on the experience of a living being that puts itself forward as the sole source of meaning, and a deliberative intelligence in the living organism with the living organism, of all with all. Debate, moving beyond the sensitivities of different factions: this is the issue. We can only hope for an extension to the much-needed training that has been started by Inf'OGM not only with all of the GMO monitoring networks, but also all those who explore the possibilities of our world. What fundamental issues need to be addressed?

- In terms of knowledge: What is genetics? What are living organisms? Once the myths of a gene republic and even greater control are done with, we ultimately arrive at the following conclusion: in biology, everything has yet to be done. Of course, there are a few ideas on the "living organism-spatio-temporal- object", but on the "living organism-in-progress" conditioning at all costs, nothing has yet been said.
- In terms of ethics: What values are at stake? What is the object of our concern: human rights (which rights?), living organisms (which living organisms?), Nature (what nature?)? And what does the plant, the object of the techniques under discussion, mean to us, and how is what is done to plants important (or not)? Finally, in terms of meaning: What matters to us, and in what kind of world do we want to live?

"A meaning, from the biological and psychological point of view, is an appreciation of values in relation to a need. And a need is, for whoever feels it and lives it, an irreducible system of reference, and for that reason it is absolute."
Georges Canguilhem, *Knowledge of Life*

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[68] Malaterre C., "Lifeness signatures and the roots of the tree of life", Biology and Philosophy, 25, 2010, pp. 643-658.

Conclusion : Do new techniques produce GMOs or not?

For actors in organic agriculture, the integrity of the cell is the basic element that should not be violated: is this new red line sufficient? Do gene exchanges and mutations occur in the same way when the cell evolves within a living organism in its natural environment, as when it is isolated in the laboratory, where is the cell subject to violent artificial stresses? This question illustrates a desire to consider plants not only as laboratory objects but as part of a broader whole, the system of Life.

Recreating in an artificial way what nature does "at random" may not be possible, since the very definition of randomness is different in both cases. In science, the random refers to anything the working of which is unknown to us and whose laws we are unfamiliar with. It should now be remembered that historically, farmers have managed biodiversity, and evolved with the latter. Each plant, each variety, was adapted to variable biodiversity, land and climate. It is in this practice of agriculture that farmers' seeds inherently draw on their variable and diverse characteristics. These are characteristics that are the opposite of those currently required (stability and homogeneity) to include a variety to be sold commercially or protect it with an NPVC and list it in the catalogue. Finally, local character is the main characteristic of a farmers' variety. It is also found in users' rights and collective rights to exchange, that farmers have formulated orally. This was done orally because this was also how laws used to evolve, alongside varieties, biodiversity, the natural, economic and social environment and farmers. The response to the question posed today on the GM or other nature of organisms the product of new techniques therefore also depends on the nature of the actors that set out to answer it.
For actors who work with local farmers' varieties, variability and diversity to stabilise characteristics of interest in variable and diverse environments are the most important characteristics. For regional breeders of DUS varieties, a legal concept was created that was validated by scientists, but which is contrary to biological realities: standardising and stabilising environments to adapt them to the lines, the characteristics of which shift as soon as they leave the environment that has been made artificial by fertilisers and pesticides.

To formalise this change of approach to living organisms, the first strategy used was to conduct non-stabilised cross-breeding of inbred lines (F1 hybrid) that forces farmers to buy their seeds each year. The second strategy was to publish a catalogue of varieties whose seeds can be sold, chosen according to criteria that have eliminated the competition of reproducible farmers' seeds. The third strategy was the creation of the New Plant Variety Certificate en 1961. Its objective was to regulate competition between seed companies in enlarged economic regions (the creation of Europe), with the catalogue offering insufficient protection for intellectual property, since it is limited to the ownership of stem lines. The NPVC allows seed breeders/multipliers/sellers to become the seller of licence fees for the use of lines. In this context, the first manifestations of genetic technologies do not change the situation, as the latter result in a diversification of line breeding techniques that result in plants with characteristics that meet the criteria of the catalogue and of the NPVC (DUS). The NPVC was developed while guaranteeing free access to resources for breeders and farmers (seed companies did not wish to impede each other by prohibiting the use of protected varieties to improve them). More fundamentally, however, for farmers working with farmers' varieties, the NPVC has legalised biopiracy; all that is required to obtain an NPVC for a given variety is a simple description of said variety. Seed companies just had to collect the varieties present in farmers' fields, then describe them using costly procedures to become their exclusive owners. Once this collection was terminated, they began to call into question farmers' free access to resources by banning farm seeds or seeking to levy royalties on them. Only a few countries (including France) authorise this use of plants containing genetic information covered by a patent for research; most European countries have not specified this in their laws and countries outside Europe (the United States, Japan) have banned it.

In 1991, the third strategy was implemented with the adoption of new rules set by the UPOV, the International Convention for the Protection of New Varieties of Plants. These rules were in response to patents obtained on genetic markers. Seed companies then created the concept of the derived "essentially derived" variety, in order to prevent a biotechnology firm from appropriating their varieties, being content to insert only one or two genes into these varieties or transform them. With the 1991 UPOV, seed companies have secured a sharing of licence fees between the owner of the initial variety and that owner of the new gene and, above all, made farm seeds counterfeits (since farm seeds are, by definition, derived from varieties sown)! But two disputes have now appeared:
1) The inability to demonstrate the counterfeit, except for genetic markers. If the farmer had an obligation to declare the origin of their biological material, the counterfeit would be visible. But nowadays, such a declaration is not compulsory, as there is no provision for this declaration in the ADPIC accords. Breeders hide behind industrial secrecy in order to avoid declaring the origin of the "material" they use themselves, and to avoid the requirement to grant consent and share benefits imposed by the Convention on Biological Diversity. As things stand, it is still up to the seed company to come up with a reason to justify a presumption of a violation of an NPVC in order to be able to start legal proceedings for counterfeit production. In Europe, discussions are currently in progress on the future obligation of farmers to provide the administration with the name of the variety used, which is tantamount to denying them their right to breed plants;
2) GMOs and illegal patents (haploidy, site-directed mutagenesis, cell fusion and cytoplasmic male sterility). Biotechnology companies that patent genes now have the techniques to detect these genes wherever they happen to be.

These techniques thus give them sufficient grounds for the presumption of counterfeiting in order to claim their royalties on farm seeds in the first year, but also in subsequent years when plant material has been preserved and reproduced by a farmer, as well as on farmers' seeds that have been contaminated by their patented genes. They also allow them to claim licence fees from the breeder who has used a variety or a genetic resource containing patented genetic information for a new breed. The problem however, stems in particular from the fact that breeders cannot obtain information on the presence or absence of patented genes in resources used at a reasonable cost. There is no public information on the species or varieties in which the patents filed with the European Patent Office are used. Thus, companies are faced with the cost of managing the surveillance of all of the patents that only multinationals with larger patent portfolios can pay for. Plant variety breeders and smaller businesses therefore find themselves in a corner, having to deal with patents that are "traps" or "illegal". Faced with this situation, consideration is given to two strategies according to the type of seed companies facing this problem:

- Breeders of DUS varieties adapted to an optimum use of chemical inputs in each main climate zone use the catalogue and certification to authorise their DUS varieties only, and to prevent the sale of freely reproducible farmers' seeds, which are confined to the level of plant genetic resources collectively stored in collections of the multilateral system of the ITPGRFA ("common heritage of humanity"). These average-sized regional companies remain wedded to the NPVC, which regulates competition between them while at the same time sharing the results of their innovations to foster future innovation. This is why they are claiming the extension of "breeders' rights" to all plants covered by a patent on genetic information. However, faced with competition from patent owners who prohibit all reproduction of "their" seeds, farm seeds become an unbearable “loss” for breeders'. For this reason, they portray the payment of royalties on farm seeds as their only means of survival in a globalised market, and as a precondition to any patent reform. This precondition has led them to reduce the "breeders' rihgts" on "patented material" to an "exemption for research", and not "for breeding", i.e. to the commercialisation of the results of research. This new commitment, which has already been included in French law, would allow them to deprive farmers of their right to the exemption for research in fields where crops are commercially grown, and to thus justify royalties on farm seeds, while at the same time protecting their own freedom to access all genetic resources available, and the commercial effectiveness of the patent. However, the debate is not over: some breeders, in particular Dutch breeders, who sell non-reproducing seeds and plants (F1 plant and flower hybrids) and who therefore are not particularly concerned about farm seeds, are not satisfied with an exemption for research and are also demanding an exemption for breeding;
- Gene modifiers who work for multinational companies wish to integrate their patented genes in as many varieties adapted to each climate zone as possible. In this regard, the companies wish to free themselves of the constraints of the catalogue, as the latter imposes periods of access to the market that are too long but are also too restrictive for their own increasingly unstable varieties, as well as the optimal development of local varieties into which they could insert their patented genetic information. Patents allow these companies to ensure that the agricultural subsidiaries remain under their control, while their resulting financial clout allows them to eliminate or absorb rivals by reinforcing rules for evaluating of products before they are released on the market (certification, health, environmental, phytosanitary, biosecurity), as well as the administrative and legal costs of managing patent portfolios.

A number of companies hedge their bets, with operations as plant variety breeders and gene modifiers, adapting their strategies to the legal context in each country. The main divide is around the question of the patent, with all small and medium-sized companies looking to claim the exemption for research in the face of direct opposition from large multinationals that do not wish to take such plans into consideration.

Ultimately, the main battle lines are clear. Biotechnology companies have filed a number of patents for genes without using them all, but to have them in reserve in the event of the need to discuss the industrial property a given new characteristic of interest (climatic, nutritional, agronomic, etc.) developed by a rival. With new genetic technology techniques, these companies have the tools to patent genes and to detect them wherever they are found. Having resolved the problem of proving examples of counterfeit plants, these companies are now campaigning for a system that will allow them to sell on a larger scale in order to recover as much of the royalties to be made from their patents as possible. The catalogue, which restricts the number of varieties sold, is therefore not a good tool for them. However, it is still a good tool for traditional European breeders, who as a result find themselves in a situation where they do not know if the variety they are working with contains a patented gene or not. They appear to have toed the line, supporting patent legislation reform as long as they are able to recover royalties on farm seeds.

At European level, discussions on reform of the catalogue have commenced. Rules requiring farmers to provide information on the varieties they use are under discussion. With regards to patents, Directive 98/44 could again be up for discussion following the reform of the NPVC and of farm seed regulations.

In terms of techniques, GMOs that are the product of transgenesis have drawn a red line for genetic “progress”. The technique used to create organisms that are sufficiently artificial to be patented has led to social debate and mass mobilisation. For 15 years, plants that are the product of transgenesis have been the focus of attention everywhere on the planet, and consequently regulatory frameworks have been negotiated (Directive 2001/18 on the deliberate release into the environment, the Cartagena Protocol for the cross-border exchange of GMOs, etc.). Multinationals, which had agreed to a reinforcement of rules on market access that allowed them to eliminate their smaller rivals in exchange for direct access to the whole European market, have not won their bet in full. However, GMOs are just the visible tip of the iceberg. Meanwhile, techniques have continued to evolve in laboratories, continuing with the same impasse. A new series of techniques have been proposed for evaluation by experts, aimed at freeing up the excessively restrictive bio-security frameworks. These techniques fall within the same intellectual framework that reduced control of living organisms to the supposed control of the genome and which serves as justification for the privatisation through industrial property rights, producing applications that pose health, environmental and socio-economic risks that are equivalent to those created by transgenesis. The final project became a reality with synthetic biology. European discussions on new techniques were to have been finalsed during 2011, the idea being that techniques that “mark” the genome would be considered as GMOs, and that those that did not, would not be considered as such. It should be noted that the delay in the response from European experts – who have been working on this issue since 2009 – bears witness to the difficulties of such expertise, whereas techno-science is advancing at a sustained rate. The debate could end up in shameful negotiations if civil society organisations do not appropriate sufficient knowledge of the techniques in question in order to be able to make the issues visible to the public.

Facing this problem, civil society movements should be able to inform on broad outlines to contribute to the debate on transgenic plants. These broad outlines, which are the appropriation of living organisms and the need to review the epistemological questioning of techniques, are addressed in this brochure. In this way, civil society has started to assert diverse positions that assert the refusal of patents on living organisms and of the NPVC in its 1991 form, which undermines the right of farmers to save, use, exchange, sell and protect their reproducible farmers’ seeds, an obligation to inform genetic technology companies of the techniques used, the introduction of a public evaluation of these techniques before they go on the market, a prohibition on the distribution of varieties that are the product of new techniques that have not been mastered, and which produce new products whose impacts are unknown, as well as measures to restrain techniques that constitute an attack on biodiversity (non-reproducing seeds, such as F1 hybrids).

Faced with this new approach to techniques and biotechnologies in general, information watchdogs and actors in the trade union movement, the broader community and the world of science have a central role to play: their efforts will determine the ability to question and to understand the dynamics of the business world, and therefore to assert the positions of actors that have had little voice in debates until now. A dynamic is also necessary to ensure that everyone has new fora in which to ask questions about the substance and open up new approaches. This is something the association "Pour l'Emergence d'une Université du Vivant" (For the Emergence of a University on Living Systems) has tried to do for a number of years. Following all technical and legal developments requires considerable investment in terms of time and energy: ultimately, it is the approach of these techniques that determines what can be achieved, and this is becoming more and more the case. There is not enough time, space or resources available to confront this approach to genetic engineering with tests, to confront all of its entrenched positions, to compare it to other possible approaches. Nowadays, new approaches to living organisms that have been ignored by research must be weighed up, since, in order to take an interest in it, presuppositions that date at least as far back to Descartes must be called into question. Compared to physics, thinking in biology has barely evolved in the last few centuries. And yet, the time of simple causalities has been over for more a century: how can we, in the 21st century, still support public policies with outdated reasoning, as if we were unaware that this was the case? How can we reasonably expose civilian populations to risks inherent to decisions made according to models that should already have been confined to the museum of theories of the past? It has now become imperative to find the means to update and develop new approaches.

Glossary

Agro-infiltration: A new biotechnology method that uses the bacterium *Agrobacterium tumefaciens* to carry the modified gene, which will be expressed in a plant cell.
Reverse breeding: A new biotechnology method that aims to regenerate parent plants using daughter plants.
Apomixie: An asexual method of reproduction used by certain plants without fertilisation and with one stage (meiosis) of the whole process for the production of modified grain. Grains produced are genetically identical to the parent plant.
RNA: Ribonucleic acid. A molecule that carries genetic information used in particular as a framework for protein synthesis.
Cisgenesis: A form of transgenesis that uses genes from the same species as the plant to be modified.
Epigenetics: An area of genetics that focuses on the influence of the environment or of other external factors on genetic expression. This influence translates into modifications that can be passed on from one generation to the next, and which are reversible.
Cell fusion: An in vitro technique for fusing two plant cells to create a single cell.
Polyploid induction: A technique that seeks to increase the number of copies of chromosomes in a cell.
Meganucleases: A sub-class of nucleases characterised by their ability to attach themselves to long DNA sequences, generally resulting in DNA being cut at a single point.
Methylation: An epigenetic modification to DNA that works by adding a chemical molecule (methyl group) to part of the DNA.
Mutagenesis: An everyday term that refers to the voluntary modification of the DNA sequence via the use of chemical or physical agents, the breeding of mutant plants in the field, or the use of oligonucleotides.
Random mutagenesis: Mutagenesis in which mutations are random both in terms of location and number. Uses chemical or physical agents.
Site-directed mutagenesis: Mutagenesis in which mutations are caused by the use of oligonucleotides, and appear in a controlled manner on site.
Nuclease: An enzyme that cuts DNA in a precise location. Several nucleases exist, depending on the DNA sequence recognised before it is cut.
Zinc finger nucleases: A sub-class of nucleases characterised by their ability to attach themselves to long DNA sequences, generally resulting in DNA being cut at a single point. These nucleases are artificial, and have a domain that consists of a finger held by a zinc atom.
Nucleotide: An organic molecule that forms the basis of nucleic acids present in cells. Nucleotides are also commonly called bases. The four oligonucleotides of DNA are thymine, adenine, cytosine and guanine.
Oligonucleotides: Short DNA sequences obtained via chemical synthesis.
Polymerisation: The production of a dual DNA strand from an existing strand and with the help of an enzyme called polymerase.
Methyl radicals: Chemical molecules added to or removed from nucleotides during epigenetic modifications.
Transduction: The transfer of DNA from one cell to another using a viral vector.

The EMERGENCE series of books of PEUV

« Pour l'Emergence d'une Université du Vivant » (PEUV) is an association, founded in 2009. Its purpose is to launch a « University of Life » that would be a place of exchange, of research and training, aiming at :
- developing our knowledge of the specific nature of life, by setting up the necessary epistemological and experimental bases, while drawing from various philosophies, and by fostering debate and meetings between different points of view.
- sharing, exchanging, welcoming and sustaining autonomous research, with a priority for a plural and collectively built knowledge.
- developing ethical principles of action, of orientation and advice, which respect the integrity of the living world, as well as the freedom of thought and initiative of all concerned researchers and individuals.

A horizontal project is composed of several events, trainings, seminars and congresses, organised by PEUV's institutions*. These gatherings are opportunities to go deeper into the following issues: new technologies applied to life and the living world, participative selection, human/plant relationship, norms and life, and global ways of approaching life. Our idea is to gather and confront a variety of different points of view that improve our approach of life. These are the basic building blocks of the future University of Life.

« EMERGENCE » is the series of books resulting from those meetings, of which the present book is part of.

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With the financial support of

Fondation Charles Léopold Mayer pour le Progrès de l'Homme

Fondation pour une terre humaine

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