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Articoli/*Articles*

THE REVOLUTIONARY IMPLICATIONS OF THE WORD BIOTECHNOLOGY

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SUMMARY

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Despite the success of the chemical industry, since the early 20th century biotechnology has been framed as a natural and revolutionary alternative. The idea has involved the interweaving of the concepts of engineering new products using living processes, and of engineering new living beings themselves. The potential of these twin themes as alternatives to chemical technologies has been debated since the revolutionary era at the end of World War 1. Highpoints included the 1930s and the 1960s. The emergence of genetic engineering techniques in the 1970s enabled the realisation of long-existing aspirations. Even since then there have been marked changes as the emphasis of biotechnology has shifted from the engineering of micro-organisms to produce proteins to the engineering of animals and even man. The sense of millenial change expressed when the human genome was first drafted is therefore both genuine and old-established.

The contemporary distrust of genetically engineered organisms and of companies that make them is freshly experienced and urgent to many – and also in a century-long tradition. Whereas today's language of "risk" is new, the atmosphere of revolt and uncertainty is not.

The drive for biotechnology has driven generations of would-be revolutionaries who have felt that traditional models of technology were out-of-date. Theirs has been a vision that has expressed hope of a new kind of relationship between technology

Key words: Human genome project - Chemical industry - Revolt - Chemistry - Agriculture

and nature — itself born of distrust. I shall suggest that this distrust has been particularly associated with suspicion of the chemical industry.

Despite the current language of risk and uncertainty, such relics of the vocabulary of modernism as "techno-science" and "modern technological civilization" still imply a harmony between experts. It is therefore worth reflecting upon the contested nature even of apparently "successful" technologies, their relationship to nature and the uncertain nature of ultimate victory. Moreover historians of technology have a habit of identifying history in a sense of periodic "revolutions." While such concepts are valuable organisational tools and powerful metaphors, we must never assume that revolutions end and dissent silenced. The first industrial revolution culminating in great industrial cities and mass production spawned objectors through the 19th century and beyond. Equally the second industrial revolution in which the design and production of novel chemicals had such an important part proved intensely controversial. No sooner had it been announced than its sequel was already forseen.

The chemical industry which had emerged in the late 19th century as the indicator of modernity had in the early first quarter of the 20th century spawned some of the world's most powerful companies. These organisations, IG Farben, Du Pont, and ICI unlike many other powerful combines were not dedicated just to maintenance of the status quo but also to radical change. During the First World War the chemical companies had produced explosives and poison gases which had become a symbol of terror. Plastics and insecticides, synthetic fibres and truth drugs presented the vision of a world by means of the crushing and replacement of nature.

For a century the industry's strength was its integrated nature, so that the same great companies made both bulk products and drugs, defoliants and domestic cleaners. The technologies of high pressure hydrogenation made ammonia and thence fertilizers. But also explosives and even synthetic petroleum. The outputs of one process could also become the inputs to another. The topography of a giant plant such as BASF's Ludwigshafen complex mirrored the network of chemical reactions in its se-

quence of plants. This integration caused difficulties, too, trouble on a wide front came to the door of the same few companies. They were accused of monopoly practices, of excessive power on governments and of making death-dealing chemicals without any moral compunction.

The chemists who felt their industry was under attack fought back by emphasizing their contributions to civilisation[1]. Books such as the magnificently illustrated *Man in a chemical world* (1937) spoke of chemists' contribution to the products and consumer goods of the modern world[2]. The new science museums each boasted exhibition spaces devoted to chemistry. The 1929 catalogue of the collection on industrial chemistry at London's Science Museum spoke out: *"Truly it may be said that the romance of applied chemistry in recent times is one that cannot be surpassed for the brilliance and far-reaching effects of the discoveries that have been made, or for the benefits that have thereby accrued"*[3]. The author was a British civil servant. Others, such as the British marxist scientist, J D Bernal, tied scientific to political revolution. This founder of British molecular biology published a book entitled *The World, the Flesh and the Devil* in 1929. Here he articulated a dream of a new world of chemistry in which old fashioned natural materials, had been replaced by the synthetic and proteins were supplemented by the products of human ingenuity[4].

The use of the word biotechnology has represented a wish to find an alternative to the chemical revolution. Throughout the twentieth century the combination of the words bio and technology was radical. Of course the detailed technical reference of the word has changed over the three generations of its use. As particular meanings have been accepted they have lost their radical connotations. Thus the idea of producing chemicals by fermentation ceased to be bizarre. However old interpretations were replaced by new meanings and the word biotechnology was repeatedly reinvigorated.

The enthusiasm and also the anxiety over biotechnology date from the First World War period in which European culture was being challenged in extraordinary ways. In his book, *The Great Transformation*, Karl Polanyi talked of the revulsion against the

market economy and its associated industry at the end of the First World War[5]. This, he pointed out, was wider than Marxism. It was predominantly political, aimed as he said against the market. In western Europe it is perhaps true that the most prevalent distrust of the twentieth century was towards capitalism as an economic system. This distrust spawned many different appeals to the tradition of socialism — from communism to National Socialism, but it was also aesthetic and psychological, aimed against an industry which discounted its environment.

The tense relationship between nature and technology in those years immediately after the War had made the word evocative and popular. The continuing revolutionary status of the word biotechnology perhaps explains the sense of novelty even today and the amnesia that leads to forgetfulness even of the antiquity of its use. It is important too in order to understand the evangelical passion of its promoters and the anxiety of its opponents.

There are two strains of thought in the history of biotechnology, both antithetical to the chemical approach. These two strands are the search for a manufacturing method for products outside the human being, and the second, the engineering of the human frame itself. We can see today the ambiguity of the phrase genetic engineering which can refer to crops but also to drugs and even to people. These two lines have not been completely separate indeed they have been repeatedly intertwined. However their relationship has changed. In this essay I shall point to five different occasions in which this distrust of the status quo was most obvious and in which the conception of biotechnology was redrawn.

The first occasion was early in the century at the time roughly of the First World War. The second was in the 1930s, the third in the 1960s and the fourth to which I will refer was about 1980. We are today living through a fifth period whose concerns centering on people are proving rather different from the issues mostly focusing upon proteins raised twenty years ago.

The German word *"Biotechnologie"* was coined during the First World War and in German dictionaries during the 1920s. The English word appeared in the early 1920s and the Italian

word Biotecnologia was used in 1922[6]. The man who coined the word biotechnology combined romance with industry. His name was Karl Ereky, Ereky Karoly in the language of his native land, Hungary. He was an engineer dedicated to the abolition of hunger. In 1910 he founded the world's largest pig fattening farm, intended to house 50,000 pigs[7]. Ereky saw the pigs as machines processing sugar beet inputs into fat and meat. He called them 'Biotechnologische Artbeitsmaschinen'. In 1919 Ereky published a book describing his philosophy for a post-war world even closer to hunger than when he had begun his work. His book was reviewed widely[8].

Ereky had used the word biotechnology almost as marketing ploy for his philosophy of industrialised farming. It was used by others also as a marketing tool for their own purposes. In Chicago, Illinois, the former brewing consultant Emil Siebel sought to describe his approach to making soft drinks in the era of prohibition. In about 1920 he called his new company "The Bureau of Bio-technology"[9].

The development of new uses for fermentation was an unexpected outcome of prohibition. A 1930 textbook designed for people formerly employed in brewing beer was dedicated to `a more complete use of the microbiological processes in industry'.[10] In Britain, a consultancy specialising in the applications of microbiology, took the same name also in 1920. It published a bulletin reporting its work. This was sent to many libraries and publications and was widely reviewed. It was even reviewed in Italian leather journals, thus introducing the word Biotecnologia into Italian[11].

The manufacture of pork, leather or beer may seem a long way from a revolution in industry tout court. However the atmosphere of the time meant that great claims could be made for small achievements and indeed great outcomes could come from apparently small beginnings. Shortly after these early visions, a failed Austrian painter was imprisoned in Germany as punishment for his pathetic attempt at a political uprising.

Ereky was an engineer at the periphery of the industrialised world. At its heart meanwhile scientists and philosophers challenged the sustainability of the technology of industrial society:

of the ever-more intensive use of non-renewable resources, of the violence of the chemical reaction, of the replacement of the living by the mechanical, chemical and electronic. This revulsion was expressed in agricultural and rural romanticism, in a new ecologism and an environmentalist sensitivity.

More radical yet than the reduction of the human to the machine, was the possibility of reconsidering the machine in terms of the living. This was of course the theme of Karel Capek's *R.U.R.* published in 1920. At first the robot dream is to replace people by machines: *"Mankind is no more. Mankind gave us too little life. We wanted more life"*[12]. However the machines are sterile. Only love and redemption enables two young robots to become a new Adam and Eve. The prospect of a technological evolution out of the era of coal and iron into a more humane technological era offered to transcend the confrontation between the heartless technocrats and the hopeless romantics.

A leader of the movement was the Scots biologist and town planner Patrick Geddes. As early as 1915 he was identifying what he called the "second industrial revolution" separating the new world of gleaming neotechnics from the world of filthy coal and iron based "paleotechnics". Neotechnics based on the use of electricity and such new materials as aluminium would in its turn be superseded. In a 1919 book he lyrically saw the first signs of a further biological world which would be based on "biotechnics":

> *"Throughout the biological sciences and their arts as applied in the faculties of Agriculture, Hygiene and Medicine, we see then a definite transformation in progress. it consists of a turning around upon the mechanical, physical and chemical science and a deliberate harnessing of these to the services of Life. From its former servitude to these preliminary sciences, Life is not only escaping, but learning to apply whip and rein to its previous master"*[13].

Geddes himself is almost forgotten today, however the works of his American protege Lewis Mumford such as *Technics and Civilization* and *The Culture of Cities* are still remembered, and he too foresaw a utopian biotechnic world. Mumford in his turn would be influential upon several generations of biotechnology[14].

One can see an equivalent cultural radicalism in the self-conscious pornography of the novel *Lady Chatterley's Lover* by D H Lawrence. This is famous for its sensuality also describes the author's revulsion against the industrial scene of the coalfield in which he grew up. Describing the attitude of his heroine Connie in *Lady Chatterley's Lover* he described how `she took in the utter, soulless ugliness of the coal-and-iron Midlands at a glance, and left it at what it was: unbelievable and not to be thought about'[15].

To some Lawrence's flight from industry seemed no option[16]. At the Chicago World Fair held the same year as the futurist cookbook was published, a specially published book promoted the idea that we were living in the "silico-plastic age" [16]. The Science Museum holds a series of gramophone records of popular lectures on physiology given by the great British physiologist A V Hill in the late 1930s. He introduced his remarks by explaining that he would convey the nature of the body as a machine:

> *"I propose to discuss the means and the machinery by which the living body moves and performs in a chemical way. Many of those to whom I speak will not be trained in physiology so I have tried as far as possible to avoid the technical jargon of that science and to present my facts and fancies and conclusions in more everyday, sometimes in engineering terms"*[17].

At the same time, biotechnology was also emerging as a way of describing the engineering of mankind itself. This represents the second of biotechnology's turning points. By the 1920s there had been a long tradition of concern about the excessive numbers of unwanted people — defined medically, by class or by race. There were also however those who wished to improved humanity rather than merely condemn it. In an era of widely experienced malnutrition, improving human did not mean just genetics. Improving the diet of pregnant women could vastly impove the health of the next generation. The Viennese social reformer and sociologist Rudolf Goldscheid saw the route to an impovement in human capital in what he called *"Biotechnik"*. By this he meant nutrition, but even he blurred the line between environmental and genetic changes. His British contemporary Julian Huxley was more emphatic about the importance of im-

proving the genetic basis of society. Huxley would promote this vision until the late1930s when nazism made eugenics politically unacceptable in Britain[18].

One might ask what there was in common during those inter-war years between the diverse uses of the word biotechnology. I would suggest it was the sense of superseding chemical technology. Ereky and Huxley used almost the same words to suggest that chemical technology had had its day and biotechnology was for the future— though for Ereky this meant engineering the processing of pigs and for Huxley the engineering of human kind.

One sees a similar urge after the Second World War. The engineering of people may no longer have been acceptable and in the era of the new petrochemical industry, plastics and atomic power, bioengineering was still marginal. Until the end of World War 2 it was conventional to believe that penicillin would ultimately be made chemically[19]. Nonetheless the engineering of other life forms was proving to be hugely exciting. The success of penicillin makers in producing a wonder drug from mould demonstrated the power of fermentation. Moreover teams at Cold Spring Harbor and Wisconsin had mutated the mould with x-rays and ultra-violet light to produce much more productive strains of penicillium mould.[20]

The Hungarian refugee and atomic bomb pioneer turned maverick Leo Szilard published a short story in 1960 entitled *The Day of the Dolphins*, Szilard imagined a better technology invented by dolphins. A year later he created a civil rights organisation, the `Council for a Liveable World'. The council identified crucial problems in human development. Szilard himself died in 1963, but his assistant and biographer John R. Platt continued its work into the 1970s. A 1972 article in *Science* called for scientists to *"identify crucial problems of the future and to work towards their solution"*[21]. Biotechnology, it claimed, would help them tackle the great problems of over-population, famine, the environment and health. Such a vision expressed a hope seen to be antithetical to `atomic' technology. It was also antithetical to the chemical industry as seen at the time.

The chemical industry had already been struggling with its image before even the publication of *Silent Spring* in 1962. Other assault had been launched on account of concerns over the pollution of air and water. The Kefauver hearings on the drug industry had portrayed the pharmaceutical manufacturers, themselves part of the chemical industry, as profiteering and ruthless. Early in 1961 the industry had already been countenancing a major public relations counter attack[22]. However *Silent Spring* with its denunciation of DDT and the whole approach to nature it represented was an even stronger cultural attack. During the 1960s, assaults on the industry would grow as it became associated with the most problematic weapons of the Vietnam War: napalm and defoliants.

Biologists who had seen the independence of physicists collapse as the atomic bomb came to dominate that science were worried about the consequences of the success of biotechnology. As early as 1963 US geneticists had begun to worry about whether the public would be more prepared to cope with knowledge of how to combine genes and modify heredity than they had been for fission a generation earlier[23]. These concerns did not however prevent progress toward the capacity to modify genes during the early 1970s.

In 1974 molecular biologists imposed upon themselves a moratorium until regulations guaranteeing safety would be in place. Those whose sensitivities had been honed during the Vietnam War felt they were not willing to endanger society and their own reputation and autonomy by a dangerous release. Their policy was carefully hammered out at the Asilomar Conference of 1975. It is true that several who supported this moratorium which lasted two years would later feel they had overreacted yet their willingness to act from within the scientific community contrasts vividly with prewar assaults from without.

It was not just in America of course that the environmental movement took hold. Germany and Japan were perhaps the countries in which biotechnology attracted the most systematic government attention. In both, ironically, molecular biology had a relatively low profile. Rather than merely the application of a particular science, biotechnology was defined as the central set formed by the overlap of chemical engineering, biology and chemistry. It was the synergy that was defined as offering the

beginning of a new economy, producing products that were human in function and energetically economical. In both Germany and Japan policy makers were driven by a sense of the inadequacy of the last generation of technologies. These were apparently maturing and the succession was far from clear. Even if electronics or space travel offered routes to the bright industrial future, these seemed to be dominated by the USA.

The German government established a programme of Biology and Technology in 1972. This was a radical departure for a country which had identified itself so closely with chemistry. The German chemical industry had been devoted to making chemicals by synthesising them from simple products not extracting them from complex soups. But at a time when increasing priority was being accorded to environmental issues, biotechnology could be shown to address them all. The Germans having already specified the human centred targets including foods and medicines which their research of all kinds would address could highlight the central role of Biotechnologie[24].

It was not just governmental regulators who were attracted by this model. In an era in which the increasingly successful opposition to the Vietnam War was highlighting the contrasting needs of society, the individual and the environment on the one hand and of the military-industrial establishment on the other, even the chemical industry could not act as if political support would last for ever. Large companies such as Mitsubishi and Bayer promoted biological solutions with considerable public profile. Both companies established special institutes that came to be well-known. Here was a minimum accommodation to the idealists' complaints couched in terms which even the most visionary could not contest. Biotechnology was also favoured by the Green tendency emerging in the 1960s. This promoted technology which would depend on renewable resources, low energy processes that would produce biodegradable products, the use of waste, and was concerned with the health and nutrition of the world.

So biotechnology was widely considered a good thing, if not necessarily profitable. It was a safely alternative culture to promote. This image nurtured so carefully through the 1970s was

harnessed to a new industry during the Second Oil Crisis of 1978-1980. US tax law was altered to favour investing in small companies. So in 1979 a stockmarket analyst at the company E.F. Hutton applied the label `biotechnology' to the small group of companies anticipating a bounty from the use of genetic engineering to make therapeutic proteins. He organised a meeting to introduce investors to the concept and was surprised by an overwhelming response. Biotechnology had been invented as an investment opportunity. E F Hutton company subsequently trademarked the word[25].

A year later the Indian scientist A.M. Chakrabarty working at General Electric was awarded a patent on a life form, a bacterium which could break down oil. He had been seeking to engineer a bacterium common in the gut of mammals which would better break down cellulose and therefore help digest waste. His vision was therefore in the long line of biotechnology. It also signalled a revolution because if a company could win such a patent, then knowledge of life could become potentially valuable intellectual property. This was a new and radical shift whose significance was clear at the time. Many nations which had not hitherto taken an interest in the technologies of life commissioned reports and investigations[26].

In the early 1980s there were widespread hopes that the protein interferon made using some novel organism would cure cancer. The dream of profits from the organism as well as from the drug drove up stocks of biotechnology companies. Other technologies sustained similar hopes. The development of monoclonal antibody technology growing out the of Nobel-Prize winning work of Köhler and Milstein in Cambridge seemed to offer new prospects for precise attacks on particular cells[27].

Biotechnology in the early 1980s was based upon hopes of medical products and high value pharmaceuticals. At the same time agricultural products were also being developed. Three early products which each raised substantial problems were bacteria which inhibited the formation of frost on the leaves of strawberry plants (ice minus bacteria), genetically modified plants including tomatoes and rapeseed, and the hormone bST produced in genetically modified bacteria and administered to cattle to in-

crease milk yields. The first to come on stream were the ice minus bacteria. These were fought through the courts in the US through the 1980s. Although they were approved after four years of controversy they have not to-date been commercialised. Genetically modified plants followed[28].

The 1986 US patent of an engineered mouse proved deeply troubling in Europe, particularly when the patent was taken over by Du Pont. The fact that the chemical industry was involved brought suspicion. It attracted the animosity of left-wingers who otherwise might have been attracted to the oppositional nature of biotechnology.

Of course it was not either version of biotechnology that emerged dominant in the 1980s. Rather it was the model of a boutique small-company based biotechnology, distinctively outside the chemical industry that came to be the model. Yet the chemical industry moved towards it, as companies such as Monsanto felt they too could benefit. So did the opposition Bernard Davis at Harvard reflected in the 1990s:

> *Those of us who were entering biology in the 1930's were very much encouraged by the essays of J. D. Bernal and J. B. S. Haldane who predicted that the age of biology would soon emerge. Equally confidently, these authors predicted a similar success of scientific planning in solving the problems of economic and political organization. Little could the students of my generation foresee that biology would mature so rapidly, while the predicted social utopia would become more distant than ever*[29].

In 1997 Dolly was cloned. In the Middle Ages, deformed creatures had been seen as monsters, portents of natural disasters. Similarly, Dolly was seen as monster, as a portent of human cloning. An intense debate emerged, much of it concerned not with the cloning of sheep which had been achieved but with the cloning of people which had not. A search with `Google' in April 2002 revealed almost 345,000 pages of material on the web in response to the words human and cloning, compared to 898,000 for cloning alone. That by the way compares to about 2 million for "space" and "man".

Max Weber writing at the time the word biotechnology was coined, reflected on the legitimacy of authority. He reflected on

the roots of legitimacy, distinguishing between power and charisma. Biotechnology and its relationship to the chemical industry can be seen in a similar light.

Throughout the 20th century the wealth of the chemical industry has given it enormous power. This has not always been sufficient however to give it legitimacy in the eyes of many. Biotechnology has often acquired the charisma to give it the legitimacy in their eyes that the chemical industry has lacked. To others of course the qualities of charisma without either power or responsibility have made biotechnology deeply untrustworthy.

Today biotechnology is acquiring power. It could be argued that in fact by the end of the 20th century, biotechnology broadly understood had decisively vanquished its old challenger the chemical industry. The pharmaceutical company Merck was now a significantly larger organisation than the erstwhile giant Du Pont which in 1940 had been 20 times its size. The chemical company Hoechst had amalgamated with Rhone Poulenc to give the pharmaceutical company Aventis, and ICI and Astra had spawned the larger Astra Zeneca with the rump of ICI now a small company. It could even be argued that the day of the integrated chemical industry making everything from simple commodity to complex drug has now passed. Certainly the manufacture of high value drugs seems more profitable.

Ironically however today as biotechnology acquires the legitimacy of power it is losing its charisma. Questions of trust continue to be its companions. With biotechnology as with other revolutionary movements, two emotions are often associated: hope but also distrust. Whether it is over genetically modified plants or the use of cloned foetal cells large numbers of citizens are uncertain of where the new technology is going. Even more perhaps than the technology itself, its proponents are distrusted. Survey after survey has shown that those organisations associated with the promotion and regulation of biotechnology — industry and governments are distrusted.

The transition of biotechnology from angry outsider to resource rich insider yet with a radical agenda is represented by the history of the human genome program. The sequencing of the human genome and its potential modification had been dis-

cussed from the 1960s. However the scale of the task seemed gigantic. The development of automatic sequencers in the 1980s and the prospect of an international race focused attention in the United States. Following initiatives from the Department of Energy and from NIH, The US government formally launched its human genome project in 1990. Plans were accelerated by the threat of competition from private companies and the US government agencies were joined by Britain's Wellcome Trust. In May 2000 almost 68,000 pages relating to the human genome project were identified by the Google browser. By 2002 incidentally the number has risen to 169,000.

The first draft of the sequence was announced on 27 June 2000, when the British Prime Minister and the American President together addressed a transatlantic press conference. An accompanying press release quoted triumphant words from the Director of Britain's Wellcome Trust. He described the day as one of the most significant dates in human history[30]. The achievement had an importance even greater than the development of the wheel. Here was an explicit model of technological evolution which had now become so commonplace that we have ceased to reflect on its significance. When we do, we hear the voice of the successor to Henry Wellcome, creator of the world's greatest collection in the history of medicine. Hail the revolution!

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Articoli/*Articles*

LESSONS FROM ANTI-THALASSEMIA CAMPAIGNS IN ITALY, BEFORE PRENATAL DIAGNOSIS

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SUMMARY

The essay reconstructs the antithalassemia campaign carried out by means of population screening and pre-marriage counselling for about twenty years in Italy, immediately after the relationship between microcythemia and Cooley's anemia had been established, as well as its genetic bases. We examine the Italian contributions to the understanding of the genetics and of the clinical treatment of thalassemic disorders, and analyze the approaches to prevention as well as the results obtained by the first campaign against a genetic disease, conceived and largely implemented in Italy by Ezio Silvestroni and Ida Bianco. We discuss the resistances met by the antithalassemia campaign due to the cultural and organizational backwardness of the Italian medical community and of the public health system. Moreover we analyse the explanations and interpretations of the problematic results of these experiences in terms of morbidity reduction. It will be pointed out that the objective of genetic counselling practised in that context assumed the concept of disease prevention at the population level, and it was far from the idea, emerged in the 1970s, of non directive genetic counselling.

Introduction

The beta-thalassemia prevention action undertaken by the health services in the early 'seventies in various countries by means of the genetic screening of the population and prenatal diagnosis, made it possible, on the basis of pre- or post-nuptial

Key words: History of thalassemia - History of genetic screening, Pre-marriage counselling, Ezio Silvestroni, Ida Bianco