Unravelling gene biotechnology

Mae-Wan Ho

In a piece of scientific advocacy, biophysicist Mae-Wan Ho *examines the theoretical assumptions behind the practice and applications of gene biotechnology. She argues that the underlying paradigm on which the industry is built is fundamentally flawed. The implications of not recognising this are serious for both society and the environment.*

Gene biotechnology is threatening to take over every aspect of our daily life, from the produce on sale in supermarkets to gene replacement therapy for *the* sick. It is hailed as the coming revolution of the twenty first century, as far-reaching as information technology has been for the twentieth. Significantly, the revolution is located (always) in the not too distant future. Gene biotechnology is big business, selling dreams and promises, none of which have yet been realised. But it is coming under increasing criticism, from many quarters, and there are growing concerns about its inherent dangers.

Many issues are raised by gene biotechnology: the ethics of genetic manipulation and the patenting of organisms; the use and abuse of genetic information; the attribution of intellectual property rights and *the* exploitation of the South by the North under *the* Biodiversity and GATT treaties; the threat

posed by biotechnology to biodiversity and the livelihood of indigenous farmers; and its hazardous implications for health and the ecological environment. Gene biotechnology represents the commercialisation of science, the enclosure of the 'intellectual commons' and the exclusion of alternative knowledge systems. It is a misuse of technology, guided by a discredited genetic paradigm which epitomises the reductionist, scientistic worldview that has shaped the politics and policies of Northern countries for the greater part of the twentieth century. (For an account of the old genetic paradigm, see pp90-2.)

In the 1970s the genetic paradigm gave rise to the science of the *new genetics* as well as gene biotechnology. But - and very few people realise this - the new genetics is antithetical to every assumption of the old genetic paradigm. The new genetics is consonant with a different paradigm - the paradigm of organic wholeness and complexity that is emerging from contemporary western science. Indeed, the present wide-ranging opposition to many aspects of gene biotechnology can be seen as a concerted struggle by supporters of the new paradigm, to reclaim holistic worldviews and holistic ways of life in both North and South.

What is gene biotechnology?

Gene biotechnology, or genetic engineering, is a set of techniques for modifying and recombining genes from different organisms. It is also referred to as recombinant DNA (rDNA) technology. DNA, the genetic material, is a very long chain-like polymer made up of many, many thousands of simpler units joined end to end. The units differ in the organic bases they contain, of which there are four, represented by the letters, A, T, C, G. The sequence in which the bases occur is specific for each DNA molecule, and this accounts for its specificity as genetic material. Each DNA molecule is packaged into a linear structure, a *chromosome.* Each cell can have one or more chromosomes; for example, a bacterial cell has one chromosome, whereas the human cell has 23 pairs of chromosomes. A gene is a stretch of DNA on the chromosome, usually about 1000 units in length.

'The new genetics is antithetical to every assumption of the old genetic paradigm'

Genetic engineering originated in the 1970s as the result of the development of several techniques. The first, DNA sequencing, allows the sequence of bases

in any stretch of DNA to be determined. The second technique is making recombinant DNA in the test tube using enzymes isolated from micro-organisms to cut and join pieces of DNA together. This enables geneticists to put foreign genes into *viruses* or *plasmids*, which are pieces of parasitic DNA that can infect cells and multiply in them, or insert themselves into their chromosome and replicate with the host cell. Hence, modified viruses and plasmids, carrying foreign genes from a donor species, can be used as *vectors* (or carriers) to transfer the genes to a recipient species that does not naturally interbreed with the donor species. The third technique is the chemical synthesis of DNA of any desired base sequence. A fourth technique, the Polymerase Chain Reaction, discovered in 1988, allows specific gene sequence(s) in a mixture to be rapidly amplified by many times, and is extensively used in forensic DNA finger-printing.

Genetic engineering since the 1970s

Soon after genetic engineering became possible, molecular geneticists in the forefront of developing and applying the techniques became aware of the dangers that pathogenic strains of viruses or bacteria could be created by recombination in the test tube. This resulted in the Asilomar Declaration calling for a moratorium on genetic engineering until appropriate regulatory guidelines were put in place.

Now, in the 1990s, the risks from genetic manipulation have become far greater. Genetic engineering techniques are ten times faster and more powerful, and the new breed of genetically engineered organisms (or transgenics), deliberately released on a large scale, are designed to be ecologically vigorous; they are therefore potentially much more hazardous than the genetically crippled micro-organisms engineered for contained use in the laboratory in the 1970s. Where is the voice of the scientists now? Although an increasing number are critical of gene biotechnology, there has been no equivalent of the Asilomar Declaration from molecular geneticists in the 1990s, no call for a moratorium. As Harvard biologist Ruth Hubbard has pointed out, many of the current top molecular geneticists either own biotech companies or are collaborating with, or working for, such companies. Gene biotechnology is the commercialisation of science on an unprecedented scale. The conflict of private and public interest is bound to stand in the way of proper assessment of need or benefit as against hazards or socioeconomic impacts.

The 'patenting of life' and the GATT-TRIPS

The commercialisation of genetic engineering has been growing steadily since the 1970s. The first corporation, Genentech, was formed - even as a moratorium was being debated in 1976 - by molecular geneticist Paul Berg, who signed the Asilomar Declaration a year earlier. The next milestone was the 1980 US Supreme Court ruling that genetically engineered micro-organisms can be patented. Then came the USA's $3 billion federally funded Human Genome Initiative, whose project is to sequence the entire human genome (the totality of the genetic material). This opened the floodgate to 'patents on life'. A long list of patents have already been granted, and many more are pending, on controversial 'inventions' such as transgenic organisms, human genes and gene fragments. There are patent claims for a human cell line established from the spleen of a patient removed as part of the therapy for cancer; for cell lines from indigenous tribes obtained - without informed consent - ostensibly for the study of human diversity; and for seeds and plant varieties taken by Northern 'bioprospectors' from indigenous communities in the Third World who freely provided the material as well as their knowledge. These patents go to feed the mushrooming biotech industry which is hungry for products and quick profit.

To facilitate patenting for commercial exploitation, the Trade-Related Property Rights (TRIPS) treaty was introduced in the Uruguay round of GATT. As one commentator has noted, this treaty 'effectively excludes all kinds of knowledge, ideas and innovations [from patenting] that take place in the "intellectual common" - in villages among farmers, in forests among tribals.'[1] Patenting plant varieties from Third World countries robs indigenous farmers of their livelihood, and can have widespread repercussions. An example is the neem plant in India, whose seed oil possesses insecticidal and many medicinal properties. It has been freely available for millenia, so much so that the health care system of the whole of India is dependent upon it. As soon as it was 'discovered' and patented, it became a scarce commodity. Its market value shot up 100-fold within two years, to put it well beyond the means of most ordinary people. A national health system is thereby seriously undermined.

The intellectual property right over genetic resources is emerging as a major

1. V. Shiva, 'Why we should say "No" to GATT-TRIP, *Third World* Resurgence *39*, 3-5, 1994.

North-South issue. It began with the enactment of an International Convention - the Union for the Protection of New Varieties of Plant (UPOV) - in the early 1960s which gave property rights to plant breeders for varieties improved through human intervention. The source material, obtained freely from the biodiverse countries of the South, was considered the 'common heritage of mankind' and hence not subject to private ownership. This gave free access to corporate interests to bio-prospect in the South, and started the process of the increasingly arbitrary categorising of 'innovation' by Northern companies, while denying the real innovative contributions of local communities.[2] Under this unfair Convention, Northern countries are allowed to take genetic resources freely from the South as 'common heritage'; the 'heritage' is then returned to them as a priced commodity. Strong protest from Third World countries led to a meeting of the FAO Commission on Plant Genetic Resources in 1987, which recognised the contribution of traditional farmers in developing the plant. But the property right was not vested in individual farmers. Instead it accrued to the farmers' governments in the form of the right to receive assistance in maintaining the genetic resources. In odier words, it became translated into the obligation of the North to 'help' the South, tied into the concept of aid and dependency that has for centuries allowed the North to exploit the South. An international gene fund was set up to concretise the farmers' rights, but the lack of contributions from Northern corporations and their governments made this fund inoperative. The TRIPS proposal is generally seen as the latest attempt to formalise the continuing piracy of Third World genetic resources by Northern biotech companies.

'Northern countries are allowed to take genetic resources freely from the South as "common heritage"'

The enclosure of the 'intellectual commons'

By defining innovation - for the purpose of financial reward through patenting - as something done within the dominant scientific tradition of Northern Europe, the TRIPS proposal effectively excludes *all* other knowledge systems, whether in the Third World, or in indigenous or folk wisdom in the North or

2.- See G.S. Nijar, and Y.L. Chee, 'Intellectual property rights: the threat to farmers and biodiversity', *Third World Resurgence 39*, 6-12, 1994.

any other alternative frameworks. Public funding for scientific research with the US, the UK and the European Community is now disproportionately biased in favour of product-oriented biotechnology, particularly in partnership with industry. While many areas of basic science are no longer funded, disciplines ranging from embryology and ecology to psychology and andiropology have one by one succumbed to the dominant reductionist mindset of genetic determinism (which, wrongly, regards genes as the most fundamental essences of organisms). The pluralistic, open enquiry that has long been the ideal of science is fast becoming obsolete. Even molecular geneticists are increasingly disillusioned within a system that judges excellence on patents owned rather than on the advancement of science.

The commercialisation of gene biotechnology is reducing the life sciences to a monolithic intellectual wasteland of genetic determinism. It is the enclosure of the intellectual commons, and a 'de-intellectualisation of civil society, so that the mind becomes [subjugated to] a corporate monopoly.'[3]

Life as commodity and the ethics of gene biotechnology

The strongest reaction to the 'patenting of life' is often that it has turned organisms, including parts of human beings, into saleable commodities. This is morally repugnant to many indigenous cultures in the Third World, and has also united in opposition diverse groups in the North, including environmental activists, socialists, and religious organisations, as well as ordinary citizens who feel that the final frontier of human decency has been breached in the name of free enterprise.

But there are many other ethical issues raised by gene biotechnology, particularly in relation to the diagnosis of genetic diseases, and, more controversially, of more general genetic 'predispositions' to various deficiencies. For example, the diagnosis of genetic disease has led to individuals being discriminated against in health insurance and in employment. This kind of diagnosis of diseases for which no cure is forthcoming is in any case of questionable value, as even for many so-called 'single-gene' diseases, the clinical prognosis can vary widely from individual to individual.

Nonetheless, geneticists are now attempting to identify genetic

3. V. Shiva, *op. cit.*

'predispositions' and 'genetic propensities' for conditions such as cancer, diabetes, and schizophrenia. Worse still are the attempts to identify genetic predispositions for alcoholism, homosexuality and criminality, all of which are overwhelmingly under the influence of environmental and social factors. (Homosexuality is, of course, only a 'problem' in the eyes of these scientists.) This not only diverts attention from the real causes of illness but also increasingly stigmatises individuals, through placing the blame of society's ills on people's genes, and through the arbitrary categorisation of 'normal' versus the 'abnormal'. The identification of undesirable 'genetic possibilities' can further extend the scope for 'therapeutic' abortions. Such 'therapeutic' abortions of affected foetuses, together with the contemplation of germline gene therapy (i.e. genetic 'correction' of human eggs and sperm) are, respectively, negative and positive eugenics measures, and are are now 'privatised' by industry. This was prophesied by marxist geneticist Richard Lewontin ten years ago.

'The life sciences are being reduced to a monolithic intellectual wasteland of genetic determinism'

Eugenic movements have played a prominent role in the politics and history of much of the present century. They have played their part in the justification of the devastation of indigenous populations by colonising Europeans, apartheid in South Africa, and the genocide of Jews in Nazi Germany. Eugenic ideology is responsible for the continuing discrimination against racial minorities and all politically dispossessed groups in the world today. Major concerns about population increase are consistently directed at human populations that are non-white; whereas the real issue is the unequal distribution of resources, most of which are disproportionately consumed by the well-to-do in the predominantly white developed countries. In addition, one cannot be complacent about the dangers of state-sanctioned eugenic practice. China has just legislated for the compulsory termination of pregnancies where the foetus is diagnosed positive for conditions including schizophrenia, where the genetic etiology remains tenuous at best.

Another ethical issue is the welfare of animals used in genetic engineering experiments to improve livestock, or as living factories for drugs, or to model human genetic diseases. As the technology is very inefficient, large numbers of animals have to be experimented on before a successful transgenic is constructed,

and then many turn out to be very sick animals even though they were not intended to be so.

Gene biotechnology and biosafety

At the same time that the GATT-TRIPS proposal was pushed through, a Chapter (16) was drafted for the UN Biodiversity Convention (Agenda 21, signed in Rio de Janeiro in 1992). It was entitled, 'Environmentally Sound Management of Biotechnology', and recommended that some billions of dollars of the UN budget be committed to gene biotechnology so as to increase food yield to feed the hungry, to improve human health and control population, to purify water, to clean up the environment, to reforest wasteland - in short, to solve all the problems of the Third World. This *comes at a time when no other UN project is being funded under the Commission for Sustainable Development.* Chapter 16 of Agenda 21 is generally regarded as a thinly veiled attempt to promote and subsidise the biotech industry. Moreover, as opposition to gene biotechnology has been gathering momentum in developed countries, the industry is targetting the Third World for test-sites as well as markets. Critics are justifiably concerned about the uncontrolled releases of transgenic organisms in the Third World, and people being used as human guinea-pigs for testing genetically engineered drugs and vaccines. There have already been at least 90 releases of transgenic crops in non-OECD countries and Mexico, a third of which were by multinational corporations.[4] A rabies vaccine containing a live virus was tested on cattle in Argentina without authorisation, and farm-workers who were not informed of the experiment were subsequently found to be infected with the virus.

Clearly, most Third World countries do not have the legal framework or the capacity to regulate genetic engineering. The same is true, however, of developed countries. There is at present no legal control over genetically engineered versions of drugs and chemicals already approved for the market, nor is there any legal requirement that they be labelled as such, despite the fact that, in 1989, a batch of genetically engineered L-tryptophan manufactured by a Tokyo-based company caused 38 deaths and 1512 reported cases of illness, referred to as eosinophilia-myalia syndrome.

The repeated claims by representatives of the biotech industry that genetic

4. I. Meister, and S. Mayer, Genetically engineered plants: releases and *impacts on less developed countries,* A Greenpeace inventory, Greenpeace international, 1994.

engineered products are beneficial, effective and safe, have not been borne out by the evidence. Over half of the transgenic crop-plants are engineered to be resistant to herbicides and other environmental poisons. Many companies are engineering resistance to their own herbicides, clearly intending to market herbicide and seeds as a package deal. These plants could easily spread as weeds or create superweeds by transferring the resistant genes to related wild-species. A genetically engineered pumpkin recently planted by farmers in the US is reported to have spread to surrounding fields and become an intransigent weed. Genetic exchanges between crop-plants and wild relatives are already well known, and have recently been documented for the genetically engineered oil-seed rape with introduced genes for herbicide tolerance. This fuels worries about secondary gene transfers to non-target species, and further diminishes public confidence in the adequacy of existing regulatory guidelines.

Another 30 per cent of the transgenic crop-plants are engineered to be insect and disease resistant. The insecticidal genes include scorpion toxin, spider venom and an extremely poisonous toxin from the soil bacterium, Bacillus *thuringiensis* (Bt). These poisons will harm non-target species as well as target species of insects. Although there is said to be no evidence that the poisons can harm species other than insects, the history of DDT is sufficient to make us wary of such claims.

A source of hazard common to nearly all transgenic plants, including some well-known brands of tomato, genetically engineered to delay ripening, and introduced to the market in the US in 1994, is the virus vector used in gene transfer, which also contains gene(s) for antibiotic resistance. This will contribute further to the spread of antibiotic resistance in disease-causing bacteria, already a major public health problem. Recent research has shown that excessive antibiotics used with intensive animal farming has caused the spread of antibiotic resistance from bacteria living in the gut of farm animals to those living in the mouth and gut of humans. Bacteria are well-known as having the capacity to pick up genes (pieces of DNA) from the environment, and to pass them onto other species of bacteria. Crop-plants are in contact with hundreds of species of bacteria both in the soil and in the air. Furthermore, plants are subject to attacks by fungi and insects, which could also act as vectors for secondary transfer of introduced genes between species that do not interbreed. In the process of such secondary gene transfers, the original viral vector could mutate

and recombine with other naturally occurring viruses or pick up other genes that turn the virus into new pathogens.

Of particular significance are genetically engineered soil micro-organisms. Soil micro-organisms play very important roles in recycling nutrients for plant growth. A strain of *Klebsiella planticola,* genetically engineered to convert woody plant remains into ethanol, has been found to have unexpected effects in drastically inhibiting the growth of wheat plants. If the transgenic micro-organism were to be released, it would wipe out entire crops.

Another case in point is the engineered rabies vaccine, which has been approved for use by the European Commission to control fox rabies. It was dropped in tests as edible bait all over Europe from 1987. The vaccine has now been found to be ineffective in controlling fox rabies, and its live virus transferable to many non-target species including human beings.

What is not sufficiently emphasised is that the viral vectors used for gene transfer are deliberately constructed so as to break down species barriers and to infect a wide range of organisms. They are designed to overcome the natural checks and balances that exist in stable, sustainable ecological communities. The scenario of uncontrollable outbreaks in viral disease cannot be lightly dismissed.

Existing guidelines are clearly insufficient to guard against hazards to both ecological and human health, as detailed investigations on released transgenics are demonstrating. These valid concerns about the health and ecological implications of gene biotechnology have convinced all Third World countries (die G77 and China), Eastern European and most Western European countries that an internationally-binding biosafety protocol for the handling and transfer of genetically engineered organisms should be established as a matter of urgency. This is openly opposed by the United States (which has as yet failed to ratify the Biodiversity Convention), on grounds that it would reduce US 'competitiveness'.

Official disinformation on gene biotechnology

The official position of the US on biosafety comes from a US National Research Council report, Field Testing Genetically Modi/ted *Organisms: Framework {or Decisions,* which states *a priori,* that 'no conceptual distinction exists between genetic modification of plants and micro-organisms by classical methods or by molecular techniques that modify DNA and transfer genes.' This is obviously untrue. Recombinant DNA techniques transfer genes, on a large scale, between

species that have no probability of exchanging genes in nature. As distinct from conventional breeding methods, where different forms of the same gene (alleles) are being reshuffled between varieties of the same species or close relatives, genetic engineering transfers *novel* genes into organisms, which are facilitated by vectors. However, there is no control over where in the genome the new genes will be inserted, which makes the effects of gene transfer highly unpredictable, as demonstrated in the transgenic experiments themselves that have already created many unexpectedly sick animals. Furthermore, the stability of the transferred genes and hence their propensity for secondary mobility within the same organism or to other organisms may be enhanced relative to genes that have been introduced by traditional breeding methods.

'The failure of the "green revolution" is now generally acknowledged'

The *a priori* assumption that there is no difference between genetically engineered varieties and varieties made by traditional breeding methods has meant that field tests are both inadequately designed and inadequately monitored for safety. (They are governed, as we are told by a defender of gene biotechnology, on the 'don't need, don't look' basis, as opposed to the 'don't look, don't see' basis.[5])

Monocultures of the mind

The failure of the 'green revolution' is now generally acknowledged. The large scale planting of genetic monocultures and the accompanying use of agrochemicals seriously eroded indigenous biodiversity and destroyed the environment; furthermore, it displaced indigenous farmers, creating wide-spread poverty. Many Third World countries have since devoted major efforts to restore the environment and to regenerate indigenous biodiversity by reviving traditional, organic farming methods which are proving to be sustainable and to have a much higher productivity than western monoculture techniques. With the hindsight of the green revolution, why is so much hope pinned onto gene biotechnology? It is the same reductionist ideology producing the same genetically uniform monocultures with the same accompanying agrochemicals. The significant difference is the added danger of genetic pollution and the

5. H. Miller, 'Don't need, don't look', Letter to the Editor, *BiolTechnobgy 13,* 201,1995.

genetic perturbation of ecosystems, which, unlike chemicals, is a self-perpetuating, self-amplifying process that will be impossible to recall.

Sustainable agriculture is increasingly practised also in Northern countries as decades of mechanisation and heavy dependence on agrochemicals have led to declining soil productivity, deteriorating environmental quality, reduced profits and threats to human and animal health. The 1989 report of the National Research Council of the US Academy of Sciences has emphasised the development and use of alternative farming systems as a means to increase productivity and decrease environmental damage, and estimates that pesticide use could be reduced by 75 per cent in ten years.

'With the hindsight of the green revolution, why is so much hope pinned onto gene biotechnology?'

There are many variants of sustainable agriculture, using a combination of modern and traditional methods, all characterised by a holistic, systems approach to understanding the complex interactions within agricultural ecologies. According to the recent surveys in the United States, sustainable agriculture not only overcomes all the problems of conventional, mechanised farming, but is also more profitable ('profit' defined as income relative to input costs).[6] As ecologist Cavalieri concludes, 'Sustainable agriculture is an essential goal for a viable future. It's time to put the emphasis on the real means that will get us there.' Despite that, the US Department of Agriculture currently provides less than $5 million to research in sustainable agriculture compared to the $90 million it has allocated to gene biotechnology.

Vandana Shiva, theoretical physicist turned political activist, has been in the forefront of the Third World's struggle (with the Third World Network, TWN) against the exploitative and destructive policies of the North. In the process, she came to realise the pervasive influence of the reductionist ideology - 'monocultures of the mind' - in shaping the policies of the North. In particular, she sees 'redefining' the life sciences as an important part of the struggle. She and Martin Khor (Malaysia), with the help of Tewolde Egziabher of Ethiopia and Brian Goodwin (Open University, UK), organised a conference on 'Redefining the Life Sciences' in Penang in July, 1994, involving scientists, social scientists,

6. J.P. Reganold, R.I. Papendick, and J.L. Parr, 'Sustainable agriculture', *Scientific American*, 72-78,]une!990.

diplomats, and political activists from 15 countries. It was an exciting and eye-opening event. A consensus among the 50 or so participants was reached by the second day. The scientists who were there took part in drafting a *Scientists'* Statement on The *Need for* Greater Regulation *and* Control *of* Genetic Engineering, which was published by the TWN and distributed at the Conference of the Commission on Sustainable Development at fire United Nations in April 1995, where a number of us also had tire opportunity to speak to policy-makers and UN delegates.

The genetic paradigm and gene biotechnology

The real irony is that there is a deep contradiction between the rational (scientific) message of the new genetics, i.e. genetics since the 1970s, and the outmoded ideology of the old genetic paradigm which continues to inform the practice of gene biotechnology, shaping its goals and aims and serving to manipulate public opinion in its favour. The new genetics makes it possible to modify genes and genomes. But it also overthrows every single assumption of the old genetics. However, the old, discredited paradigm is pressed into the service of selling gene biotechnology, and to formulate policies on gene biotechnology. Paradoxical as it may seem, gene biotechnology is possible precisely because the old genetic paradigm is widely recognised as invalid. Thus, many of the promises of gene biotechnology can never be fulfilled because the genetic paradigm is an erroneous, reductionist representation of organic wholeness and complexity. The many problems which have arisen with gene biotechnology are indicative of the fundamental error in judgement on the part of those who see gene biotechnology as the solution to all the problems that humanity faces today. If further evidence is needed, biotech stocks are currently in the doldrums. According to a report in *Business Week,* 'The industry is still peddling dreams... From Wall Street's perspective, "the industry hasn't worked, and the likelihood of success is lower".'[7] A long list of products have failed clinical trials, and even the remaining handful that have got through are not without problems.

Financial ruin is perhaps a small price to pay for misjudging gene biotechnology, when the future of the planet and all its inhabitants are at stake. The

7. J-O'C. Hamilton, and J. Carey, 'Biotech. An industry crowded with players faces an ugly reckoning', Business *Week,* 66-72, 26 September 1994.

dangers of the mismatch between a powerful set of techniques and an outmoded, discredited ideology guiding its practice should not be underestimated. This mismatch also constitutes the major stumbling block to a rational debate on gene biotechnology and its legitimate spheres of application. With that in mind, let us look at the genetic paradigm and the new genetics in turn.

What is the genetic paradigm?

A 'paradigm' is a comprehensive system of thought and practice developed around a key idea or theory. A scientific paradigm is obviously built around scientific theories, but it can be so pervasive that it spills over into all other disciplines, and permeates the popular culture at large. The genetic paradigm is of this nature. It portrays genes as the most fundamental essences of organisms. It supposes that while the environment can be molded and reshaped, biological nature in the form of genes is fixed and unchanging and can be sorted from environmental influence. Further, it assumes that the function of each gene can be defined independently of every other. It is on such a basis that the Human Genome Project promises to unveil the 'genetic programme' for making a human being. James Watson, the first Director of the Human Genome Organisation (HUGO), set the tone, 'We used to think that our fate was in the stars. Now we know, in large measure, our fate is in our genes.'

The twin pillars of the genetic paradigm are Darwin's theory of evolution by natural selection and the gene theory of heredity as developed by Mendel, Weismann, Johannsen and others. Darwin proposed that evolution occurs by natural selection, in which nature effectively 'selects' the fittest in the same way that artificial selection practised by plant and animal breeders ensures that the best, or the most desirable, characters are bred or preserved. The ideology of natural selection is clear: those that survive to reproduce, those that do well, are naturally favoured with superior qualities that can be passed on, like a legacy, to the next generation. In the same way, those with inferior qualities are eliminated. Darwin's theory lacked a mechanism of heredity and variation. This was supplied by Mendel, who proposed that the (Darwinian) qualities inhere in constant factors (later called genes) which determine the organisms' characters, which are passed on to the next generation during reproduction, and variations are generated by rare random mutations in those genes. The combination of Mendelian genetics and Darwinian theory resulted in the 'neo-Darwinian' synthesis.

The demise of the genetic paradigm and the new genetics

The genetic paradigm today is neo-Darwinism writ large. Thus, everything from IQ to philandering in human males can be explained by invoking a gene or genes responsible, which can be selected for or against. And so geneticists can hunt for them in the genome.

There are three basic assumptions of the genetic paradigm:

1. Genes determine characters in a straightforward or additive (i.e. noninteractive) way.
2. Genes and genomes are stable, and except for rare random mutations, are passed on unchanged to the next generation.
3. Genes and genomes cannot be changed directly by the environment.

All three assumptions have been demonstrated to be false.

Assumption one contradicts everything that is know about metabolism and genetics for at least 40 years. Organisms including human beings have tens of thousands of genes in their genome. Each gene exists in multiple variants. One of the main functions of genes is to code for the thousands of enzymes catalysing thousands of metabolic reactions in our body which provide us with energy to do everything that constitutes being alive. These metabolic reactions form an immensely complicated network in which the product of one enzyme is processed by one or more other enzymes. Thus no enzyme (or gene) ever works in isolation. Consequently, the same gene will have different effects from individual to individual because the other genes (in the 'genetic background') are different. So-called 'single-gene defects' - which account for less than two per cent of all human diseases - are now proving to be very heterogeneous. Many different mutations of the same gene, or of different genes, may give the same disease, or not, as the case may be. This has been known for sickle-cell anaemia, common in in people of ethnic African origin, and more recently, for cystic fibrosis, common among Northern Europeans, and for a conglomerate of 'craniofacial syndromes' which includes achondroplastic dwarfism. All this has provoked a geneticist reporting in *Nature Genetics* to declare that there is 'no such thing as a single gene disease.'[8]

The extent to which the effect of single genes is entangled with that of all the

8. J.J. Mulvihill, 'Craniofacial syndromes: no such thing as a single gene disease', *Nature Genetics* 9,101-103,1995.

other genes really comes home to us in the findings of the new genetics. These findings not only further discredit assumption one, but also fatally undermine assumptions two and three - that genes or genomes are unchanging and do not respond directly to the environment.

The picture unveiled by the new genetics is an incredibly complex and dynamic catenation of cellular and genetic processes, many of which serve to destabilise and alter genomes within the lifetime of the organism. This is in direct contrast to the static linear conception of the 'Central Dogma' of molecular biology that previously held sway. The Central Dogma states that the genetic material DNA makes RNA in a faithful copying process called *transcription.* (RNA is ribose nucleic acid. It is similar to DNA except for the extra oxygen atom in each of the units making up the polymer.) The RNA then makes a protein by a process of decoding called *translation.* There is strictly a one-way 'information flow' from the genetic message coded in the DNA to RNA to protein, and no reverse information flow is possible (Fig. 1a). In other words, proteins cannot determine or alter the transcribed message in RNA, and RNA cannot determine or alter the genetic message in DNA. We shall see that such reverse information flow not only occurs, and in a wide variety of forms, but is, furthermore, a necessary part of how genes function within a metabolic' epigenetic supernetwork (Fig. 1b).

'The genetic paradigm today is neo-Darwinism writ large'

The Fluid Genome and the New Genetics [9]

A complicated network of feed-forward and feedback processes has to be traversed just to express one gene or to make a single protein. Genes, especially of 'higher' organisms, are found to exist in bits, and the bits must be correctly joined together to make the 'messenger' RNA. Numerous other proteins take

9. Details are to be found in the following publications: J. Pollard, 'Is Weismann's barrier absolute?', in *Beyond* Neo-Daruunism. Introduction *to the New Evolutionary Paradigm,* M.W. Ho and P.T. Saunders (eds.), Academic Press, London 1984; M.W. Ho, 'Evolution by process, not by consequence: implications of the new molecular genetics for development and evolution'. *Int. J. Comp. Psychol 1,* 3-27,1987; J. Rennie, 'DNA's new twists', Scientific America, 88-96, March 1993; E. Jablonka, and M.J. Lamb, *Epigenetic Inheritance and Evolution: The Lamarckian Dimension,* Oxford University Press, Oxford 1995.

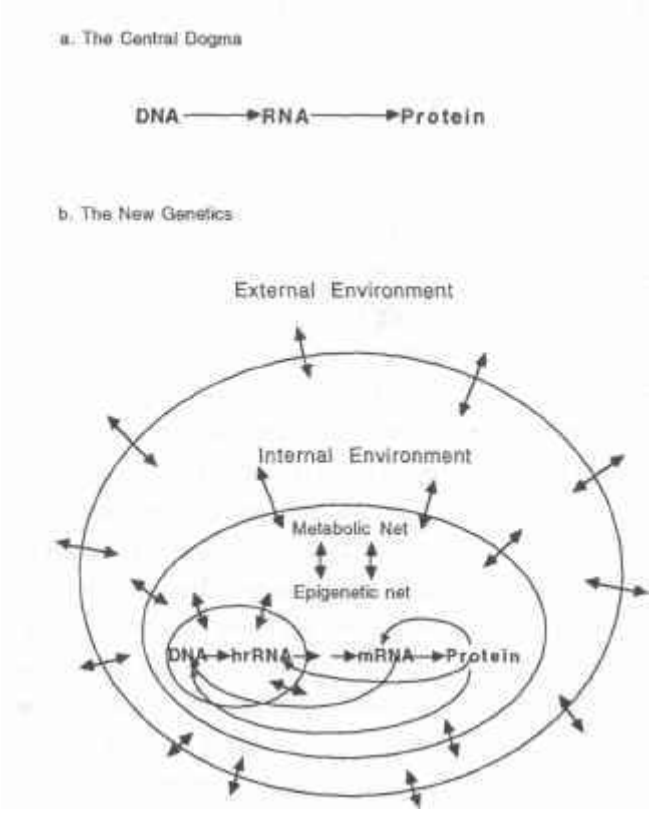

Figure I. Genetics old and new

part in making every single protein in chopping and changing, editing and recoding in a complicated *epigenetic* network which interposes between the genes and the metabolic net, and interlocks with it, forming an epigenetic-metabolic supernetwork. *It becomes increasingly difficult to define and delimit a gene, as the metaboli-epigenetic supernet ultimately connects the expression of each gene with that of every other.*

The genome, embedded as it is within the epigenetic-metabolic supernet, is far from stable or insulated from environmental exigencies. A large number of processes appear to be designed especially to destabilise and alter genomes during the life-time of all organisms, so much so that molecular geneticists have been inspired to coin the descriptive phrase 'the fluid genome'. Genes can be marked

by chemical modifications, base sequences can mutate, stretches of DNA can be inserted, deleted, or amplified thousands, and tens of thousands, of times. The sequences can be rearranged or recombined with other sequences, genes can jump from one site to another in the genome, and some genes can convert other genes to their own DNA sequences. These processes keep genomes in a constant state of flux in evolutionary time. Genes are found to have jumped between species that do not interbreed, being carried by mobile genetic elements, viruses or micro-organisms, which can exchange genes at a prolific rate, as witnessed by the rapid horizontal spread of antibiotic resistance in bacteria. Parasites that infect more than one species are also vectors for horizontal gene transfer. A particular genetic element - the P-element - has spread to all species of fruitflies in the wild within the span of less than 50 years, probably carried by a parasitic mite. Jumping genes, viruses and vectors for gene transfers are all related genetic parasites. They can help one another jump or mobilise, mutate, exchange parts and infect each other's hosts as a result. As I have already indicated, the vectors used to transfer genes are designed especially to overcome species barriers and to be used for a wide range of hosts, which would speed up and amplify the process of genetic exchange enormously. The genetic perturbations from large scale environmental releases of transgenetic organisms are therefore orders of magnitude greater than those normally experienced in ecological communities. Ecological systems are stabilised by a complex of natural checks and balances, of positive and negative feedback interactions, which, when sufficiently perturbed, will break down in a catastrophic manner.

'Ecological systems, when sufficiently perturbed, will break down in a catastrophic manner'

The fluid genome processes in the living system are likewise subject to physiological and cellular regulation, which can also be disrupted by the gene transfers, leading to highly unpredictable effects, as we have seen with transgenic plants and animals. On the other hand, gene jumping, recombination and other alterations of the genome have been found to be also part of the normal physiological response to environmental stress or starvation. Thus, transgenic crop-plants and other organisms will be much more prone to mobilise their transferred genes in the event of drought and other environmental stress, increasing the likelihood that they will spread to non-target species.

Most provocative of all, there is now abundant evidence of (previously forbidden) reverse information flow in the genomes of all higher organisms. Predictable and repeatable genetic changes have been found to occur simultaneously and uniformly in all the cells of the growing parts in plants exposed to different fertilisers, and the changes are inherited in subsequent generations. Similarly, plants exposed to herbicides, insects to insecticides, and cultured cells to drugs, are all capable of changing their genomes repeatedly by mutations or gene amplifications that render them resistant to the noxious agent, which is why resistance evolves so rapidly, even without the help of transferred genes introducing the resistance. And as long as high levels of herbicides are used with the herbicide-resistant transgenic plants, or high levels of insecticides are expressed by the insect-resistant crops, then some weeds and some insects will be bound to evolve the appropriate resistance, rendering the transgenic plants useless - and with disastrous ecological consequences besides.

As a final blow to the genetic paradigm, starving bacteria and yeast cells are now known to respond directly to the presence of (initially) non-metabolisable substrates by mutating the genes required to use the substrate. The genetic responses are so specific that they are referred to as 'directed mutations'.[10] In summary, genes are neither stable nor immune to environmental influence. On the contrary, they mobilise and mutate as part of the physiological response of the organism to environmental change.

Implications of the new genetics for heredity and evolution

The genetic paradigm has collapsed under the weight of its own momentum in the findings of the burgeoning new genetics. The genes are far from being the constant essences of organisms, whose effects can be neatly separated from one another or from the environment. There is furthermore, no constant genetic programme or blueprint for making the organism, for the genome can also change even as the organism is developing. How should we see heredity in the light of the new genetics ? If the genome itself is so dynamic and fluid, where does heredity reside? It is clear that heredity does not reside solely in the DNA of the genome. In the first instance, it resides in an epigenetic cellular state - a dynamic equilibrium between interlinked genie and cellular processes. But even that is an

10. See note 9, p92, for details.

abstraction and reification. It cannot be assumed that heredity is exhausted at the boundary of cells or organisms. For as organisms engage their environments in a web of mutual feedback interrelationships, they transform and maintain their environments which are also passed on to subsequent generations as home ranges, cultural traditions and artefacts. It is this whole complex of dynamical interrelationships that gives rise to the stability and repeatability of the developmental process, which we recognise as heredity.[11] The fluidity of the genome is *necessary* to the dynamic stability of the system, for genes must also adjust as appropriate to the whole.

What implications are there for evolution? just as interaction and selection cannot be separated, so neither can variation (or mutation) and selection, for the 'selective' regime may itself cause specific variations or directed mutations. The organism experiences its environment in one continuous nested process, adjusting and changing, leaving imprints in its epigenetic system, its genome as well as on the environment, all of which are inherited by subsequent generations. Thus, there is no separation between individual development and the evolution of future generations. In that respect, our fate is neither written in the stars nor in our genes, for we are *active* participants in the evolutionary drama.

The new genetics that underpins gene biotechnology belongs with a paradigm of organic wholeness and complexity which is emerging in many areas of contemporary research in the west, which is reaffirming the universal wisdom of traditional indigenous cultures all over the world.[12] However, the new genetics can give no justification to *simplistic* ideas on the capacity of organisms or ecosystems to adapt to any and all new circumstances. Organisms and ecosystems are complex dynamical systems with positive and negative feedback mechanisms that make them resilient as well as resistant to change. However, as mentioned above, these same mechanisms will also cause them to break down when the disturbance is large enough. And when they break down, they tend to do so in

11 .Directed mutation is now accepted even by some of its former strongest critics, for example, N. Symonds, 'Directed mutation: a current perspective', J. theor. Biol. 169, 317-322,1994- However, some committed neo-Darwinists still will not admit it exists.

12,This ideal is satisfied when the system is coherent. For the biophysics of coherence, see M. W. Ho, *The Rainbow and the* Worm: *The* Physics of Organisms, World Scientific, New Jersey 1993; also M.W. Ho (ed), Bioenergetics, S327 Living Processes, Open University Press, Milton Keynes 1995.

a catastrophic, spectacular fashion. The appearance of novelties and of mass extinctions alike in evolutionary history are but two sides of the same coin; we cannot be complacent about the capacity of organisms or ecosystems to adapt to any and all environmental insults that are perpetrated. The challenge is to chart the safe and sustainable uses of gene biotechnology within the new holistic paradigm.

The struggle to reclaim holistic ways of life

The collapse of the genetic paradigm is both, symptomatic and symbolic of the collapse of the reductionist worldview. The implications for gene biotechnology and biosafety are clear. The reductionist aims and assumptions in the current practice of gene biotechnology are misguided. The promises can never be fulfilled because they are built on false and discredited premises. Many of he products are not only useless but are bad for health and dangerous. They are made on the erroneous assumption that genes are stable, that their effects can be localised and specifically targetted in the tangled web of living processes.

The Harvard Working Group on New and Resurgent Diseases has just presented fresh evidence that diseases such as tuberculosis, malaria, cholera and yellow fever are still a major cause of death in many parts of the world, and hat these diseases are returning to regions where they were on the decline. New diseases also continue to emerge at unprecedented rates, from social conditions and environmental disturbances that enable pathogens to gain access to new host populations, or to become more virulent in immunologically weakened human hosts that suffer from poverty and malnutrition. Many of the agents of infectious diseases rapidly develop resistance to drugs and chemicals, and new variants continue to arise that escape he protection of vaccines - as we would expect, from what we know of the fluid genome. The Harvard Group's conclusion is hat, 'Disease cannot be understood in isolation from the social ecological, epidemiological and evolutionary context in which it emerges and spreads. Indeed, if one lesson has emerged from he spectacular failure of western medicine to 'eradicate' certain diseases, it is hat diseases cannot be reduced to a single cause nor explained with the prevailing linear scientific method: complexity is heir hallmark.[13]

13. The Harvard Working Group on New and Resurgent Diseases, 'New and resurgent diseases. The failure of attempted eradication'. *The* Ecoiogist *25,* 21-26, 1995.

In opposing the patenting of life, French geneticist Daniel Cohen, a prominent figure in the Human Genome Project, made the unprecedented move of offering a wide range of DNA sequence data obtained in his laboratory to the United Nations as the property of humanity to use freely for any appropriate purpose. Another hopeful sign is that in early 1995 the European Parliament has voted against patenting life, at least in principle, by a substantial majority.

The debate over gene biotechnology is not about disembodied, objective, ivory-tower scientific knowledge. Knowledge is what people live by. The western ideal of being 'objective' is misplaced, for it implies that one must be a completely detached, unfeeling observer outside nature. Within *the* participatory framework of other knowledge systems, the ideal of objectivity in knowledge is to be maximally communicative and connected within the nature that is the object of our knowledge, which we, as both knower and actor, participate in shaping. The present opposition to gene biotechnology is thus a concerted struggle to reclaim holistic worldviews and holistic ways of life, which are spontaneous, pluralistic, joyful, integrative, constructive and life-sustaining.

I wish to thank Martin Khor, Vandana Shiva, Gurdial Nijar, Chee Yok Ling, Ruth McCoy, Vicky Tauli-Corpus, Tewolde Egziabher, and many other members of the Third World Network for ideas that are contained in this article, and for their constant support and encouragement. I am also grateful to Brian Goodwin and Peter Saunders for helpful discussions and key references and to Doreen Massey for suggestions to improve the manuscript.