



Creating new species: the future of man and his dominion over other animals

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In my next two lectures I intend to consider some possibilities as to where modern biology may lead us during the course of the next century. Exactly what can and will be achieved in this kind of time frame is difficult to judge although the pace of scientific advance in the second half of the last century argues that by the end of the current one much of what now seems entirely the product of science fiction will have become a reality. The resultant increase in ethical debate as we struggle to deal with the consequences of scientific endeavour will represent a significant challenge.

When one asks what potential human discovery will be likely to have the greatest impact on life on this planet during the current century there are probably many things that might spring to mind. These could, for example, be to do with helping save our very existence through control of pollution, use of weapons and our predisposition for resorting to warfare. They could be improving our ability to control or even eradicate current life-threatening diseases, being able to prolong our useful lives or develop more intelligent computers and machines to help us in our every day lives. Perhaps we might even start to visit and colonise other planets. However, arguably the most challenging discoveries will be those that could allow us to design and create new life forms for our own purposes.

Plant and animal species and extinction rates

One almost inevitable consequence of progressive human population expansion and requirement for increasing areas of our planet for use by our species must be a further increase in the extinction rate of other species of life. If we fail to control our generation of toxic pollutants the process will be further accelerated. While recent global and EU agreements to reduce or even stop loss of biodiversity by 2010 are encouraging such laudable ambitions will be both difficult to achieve and even to monitor – especially given the fact that the vast majority of species living on the planet have yet to be identified.

In the big scheme of things loss of biodiversity may not seem that important. After all there are so many different species of life on the planet that we don't even have an accurate estimate of how many there really are – probably somewhere between 10 and 50 million at least. Although the vast majority of these are plants and insects we would normally have scant interest in even though they all play a role in maintaining our planet's ecosystem.

Actually it is amazing to think that despite man's enquiring mind and fascination with discovery, in the 230 years since Linnaeus began classifying all the forms of life on earth only around 1.55 million have been identified. Global estimates of 10-50 million are based on a number of different complex extrapolations from detailed observations on specific classes of species, or particular forest habitats, and involve a massive scale up and use of assumptions that result in a wide range of estimates. The bottom line is that

perhaps 90% of all plants living on the planet have yet to be identified let alone many millions of insects. Of course in terms of large land-based animal species that we tend to take more notice of, there are probably relatively few that remain to be discovered. The 5,416 species of mammals, 9,917 birds and 13,906 reptiles and amphibians represent a tiny fraction of the planet's biodiversity (compared with estimates of between 7 and 35 million insect species – 950,000 currently identified). Even fish only account for around 28,500 species with crustaceans at 40,000 and molluscs at 70,000. One interesting approach to estimating total species numbers has in fact been to back-predict from numbers of large animals on the planet how many smaller undiscovered ones there are. May (1978,1988) has published estimates based on a simple equation predicting that the proportionate numbers of species increase in a linear relationship with decreased body size to again come up with an estimate of between 10 and 50 million species.

Mass species extinctions are nothing new of course for this planet and scientists consider that the current wave triggered by human activity is the 6th great extinction in its history. There is also a natural level of extinction as habitats change and species compete with one another and this, along with previous mass extinctions, has meant that of all the species that have ever lived on this planet probably 98-99% have become extinct and therefore those still present represent a mere 1-2% of the historical spectrum of different life forms. The average duration of any particular species inhabiting the planet has been estimated to be around 10 million years. Even if we take the low total species number of 10 million this means that somewhere between 1 and 10 species will become extinct each year from natural causes. This comes out at a natural extinction rate of between 0.00001 and 0.0001% of species each year or between 0.001 and 0.01% each century. However this would be expected to be counterbalanced by the evolution of new species leading to no net loss of biodiversity.

In this current 6th wave of extinctions, rates are running at around 0.01% each year and 1% each century although for mammals it is much higher than this. The IUCN Red List of threatened species currently considers that 20% of all mammals are already under threat. This overall level of extinction rate could equate to a staggering estimate of perhaps 100-500,000 species becoming extinct every one hundred years (perhaps 1000-5000 each year). This is approximately 100-1000 times higher than the likely natural extinction rate and at the current level of the human impact on planetary environment it seems almost inevitable that it will increase many more fold by the end of the current century. Natural evolution will not generate new species at this rate and so biodiversity will decrease progressively.

The human impact

The world's human population now exceeds 6 billion having increased some 6-fold in the last 150 years. It has been estimated that this is about 30 times larger than our population would have been if we had not adopted agricultural practices.

While hunting activities have been responsible for extinctions of a number of species, especially of large mammals and birds, the major impact has been through habitat loss and degradation caused by the activities of a growing and increasingly resource hungry human race. We are now in a situation where 50% of all plant and animal species are living in closed tropical forests and the sizes of these are decreasing progressively and population increases in and around these areas are increasing faster than in other more developed regions which support much smaller numbers of species.

Of course advances in species preservation through freezing, maintaining life collections or other techniques may help prevent some species from being entirely lost and maybe we will have the ability to reconstruct a species simply from some of its DNA in true Jurassic Park style. However, the problem that made the species extinct in the first place will remain and so this will merely be a biological catalogue of life that has existed on earth and will be unlikely to reverse extinction rates of naturally supported species. We would in a sense merely be the keepers of a biological library.

So what has all this to do with major discoveries in the 21 st century you may ask? The simple answer to this is that we will almost certainly have the ability not only to modify the genomes of existing species to help them try to adapt to whatever environment we can afford to give them, we may actually also be able to create entirely new species that are deliberately engineered to help us and survive on a humanised planet. Of course there are some scientists who question seriously whether the human race will survive as a dominant force on the planet for longer than the current century and there is always the chance than an environmental catastrophe might occur. However, let us assume for the time being that these two outcomes are simply a possibility and that we must consider most seriously what might happen if things continue more or less as they are and humans continue to dominate the planet's resources.

What do we need other living species for?

Before we start to consider what humans might want to design in terms of new species we need to step back for a minute and consider our own relationship with other species, why we need them and what it is that brings us closest to them. While the same questions can be applied to all living things I will focus mainly on animals.

As I have already indicated, it goes almost without saying that it was the shift from human hunter/gatherer societies relying on natural provision of resources to farming strategies, where man has grown and maintained his own food and protection resources that have allowed the human race to expand to its current size.

For many, of course, animals provide a source of both aesthetic pleasure and a sense of wonder at their diversity. However, arguably we can derive the same from works of art and while the world would be a poorer place if we were to experience the total loss of such art, it would be unlikely to threaten our survival in a major way. A major loss of biodiversity would on the other hand have a significant impact.

If one considers the main areas where the presence of animals, our exploitation of them and our interactions with them would suffer most from their absence these would include:

Maintaining our ecosystem

Food

Labour saving assistants

Human biomedical advances

Pleasure and companionship

Psychological and emotional well-being

When you think about it, apart from the ecosystem maintenance - which is naturally of major importance – the rest of these areas with the most direct relevance to humans probably involve less than a hundred species and if one excludes food this reduces down to perhaps only around a few dozen or so.

To some extent we have already moved beyond the use of animals as labour saving assistants in the majority of the world as mechanical devices have taken over. In theory perhaps we might even be able to find artificial means of maintaining our planet's ecosystem. Our most direct need for other species may therefore reside in food production, human biomedical advances, pleasure and companionship and

psychological and emotional well-being.

Food production

The domestication of agricultural animal species to satisfy human requirements for food has been going on for many thousands of years and this, along with food crops, is a clear example of using human rather than natural selection to produce end products that meet our specific needs. This is not to say of course that any of the species involved have reached a point where no improvements- from a human use point of view – could be made. The ever increasing human demand for food makes agriculture into a high production, low space utilisation programme that is often at odds with concern for the quality of the lives of animals used or with the quality of the food produced by high yield plants requiring chemical additive support through fertilisers and pesticides. Arguably therefore there is potentially room for the generation of animal and plant species that overcome some or all of these problems. What we do know for sure is that low intensity, organic farming practices are insufficient to support the food requirements for the whole of the developed world at least, even were food produced this way to become more affordable there is insufficient land mass.

Human biomedical advances

Whichever way you want to look at it the vast majority of major medical advances in the last few centuries have relied on work carried out by us using other species. This will remain the case for some considerable time until we have achieved sufficient understanding of complex biological systems to model their functions using non-living computer-based in silicosystems and/or appropriate non-sentient organic systems – or a combination of the two. As with agriculture, ethical concerns are raised in relation to current use of complex, sentient animals for this type of research benefiting human health. While there is also a potential for creating new species where this is less of a concern, the idea of trying to produce non-sentient species is, for most, a totally unacceptable option.

Pleasure and companionship

Certainly with human adoption of fixed settlements and farming, and probably even before this, our race has done something that is rarely seen with other species, we have deliberately involved members of some other species in our societies. Some would argue that in some cases this choice was not ours but that of animal species which saw the potential to exploit the advantages afforded by human settlements – dogs for example.

Human relationships with companion animals may date back at least 10,000 years as far as dogs are concerned and 4-5000 years for cats. It is generally thought that the rich pickings produced by human settlements attracted both species to seek proximity with us and both were tolerated because of their impact on vermin control, security and even hunting activities. However, the utilitarian advantages of these companion species have become replaced progressively by their ability to become incorporated socially into human family groups. This, combined with their apparent affectionate nature, playfulness, individuality and intelligence has cemented their inclusive position in the majority of human societies and their numbers are increasing steadily.

In the UK current estimates are that there are around 15 million dogs and cats (around 7 million dogs and 8 million cats) and around 30 million other pet species (horses, rabbits, rodents, birds, fish and a host of other more exotic species). In the USA there are a staggering 137.5 million dogs and cats (76.8 million cats and 60.7 million dogs).

With our current population of around 60 million that places the pet/companion animal population running at around three-quarters of the human population. Approximately 11,000 UK households (around 38%)

have one or more cats and dogs and since 1995 the growth rate for ownership of these species is 18.5% for cats and 6.8% for dogs. In the US 36% of households have dogs and 32% have cats. In 2001 the annual value of dog and cat food shipped by the US alone was \$9.2 billion (around £5.7 billion). In the UK the size of animal medicine's industry in 2001 was £359 million and of this 53.6% was for companion animals and this particular sector of the market is the only one in animal health that is increasing.

The hunting skills of our cats in particular has meant that their growing population is having a significant impact on wildlife with claims that they are responsible for killing in the region of 10 million wild birds in the UK alone each year – a good reason why perhaps collars with bells on them should be more popular than they are.

Leaving aside the emotional support that animals can give us, which I will discuss in a moment, we have an amazing interest in many different animal species. Wildlife programmes, safari parks and wildlife centres, even zoos, all have a clear fascination for us. Sometimes it is almost as if contemplation of other animals gives us insights into our origins and a link with the natural world that the artificial environments we have managed to create for ourselves have all but destroyed. There is, of course, a dangerous delusional form of romanticism here and we are prone to see things in other species that are likely to be more the product of our fertile imaginations than an actual reality. Our media, entertainment, literature and art are full of humanised animals and we anthropomorphise to such an incredible extent that the startling conclusions which can sometimes be reached by painstaking scientific enquiry as to what other animals are capable of thinking, feeling or doing often seem pathetically mundane.

Physical, Psychological and emotional well-being

Our contact and relationships with other animals may extend far beyond simple pleasure and enjoyment however. Such interactions are increasingly recognised as providing key emotional and psychological support and even education for both adults and children. Surveys have reported that the strong psychological and emotional attachment (termed “human-animal bond”) between people and their pets enhance the quality of family life by minimizing tension between family members and enhancing compassion for living things. Animals are also being used more and more for therapeutic purposes in both human mental and physical disorders in what has been termed “animal-assisted therapy”. This has been tried, with varying degrees of scientific rigour in assessing results, for around 25 years, although the origins of individuals being deliberately exposed to animals for therapeutic purposes can be traced back many hundreds of years. So what benefits have been claimed from our interactions with other species?

Cardiovascular disease and blood pressure

One of the first main studies to show a relationship between pet ownership and human health was in relation to recovery from heart attacks. A study by Friedman et al (1980) found significantly increased survival rates after a year of having a heart attack in patients that owned pets. Subsequent studies have supported conclusions that pet ownership helps both to reduce risks of coronary heart disease and improve the chances of long-term recovery following heart attack (Anderson et al, 1992; Petronek and Glickman 1993). The largest study on 5700 individuals in Australia showed that male pet owners had significantly lower systolic blood pressure and triglyceride and cholesterol levels and also females over 40 had lower blood pressure and triglyceride levels (Anderson et al, 1992).

Minor health problems

Serpell (1991) has also reported that when he compared adults before and after they acquired pets the change was associated with a significant decrease in minor health problems. Siegel (1990) has reported that dog ownership reduced visits to doctors by the elderly by 16%.

Stress, anxiety and depression

Allen et al (1991) found that women experienced more profound reductions in their stress levels compared with being in the presence of their best friends or spouses. Similar positive effects in reducing anxiety have also been reported in institutionalised psychiatric patients (Barker and Dawson, 1998) and for individuals about to receive electroconvulsive shock (ECT). A study has even reported stress reducing benefits of tanks of tropical fish in dental surgeries! Individuals with depression have also been shown to have enhanced mood following interactions with dogs and this correlated with increased levels of amino acid precursors in their blood which promote production of brain chemicals that are associated with pleasure and euphoria such as serotonin and dopamine. Indeed, the possible adage of “try a pet rather than Prozac” might spring to mind.

Naturally the beneficial effects of companion animals for relieving stress, anxiety and depression are offset to some extent by the opposite effect that the death of a pet can have on its human owner's. This can be particularly devastating for elderly humans living alone. It is perhaps no wonder therefore that considerable interest has been expressed in cloning in relation to companion animals. This has already been achieved with cats and, even though the belief that the cloned individual will have all of the same key behavioural and physical characteristics of the original one is actually incorrect, is likely to increase in popularity as it becomes more affordable.

Recovery from trauma

Barker et al (1997) have reported that pets provide a strongly supportive role in childhood sexual abuse survivors. Furthermore, Nebbe (1998) has reported that survivors of such abuse who had a strong animal bond were likely to show less abusive behaviour and lower anger levels as adults.

Affective disorders

An area one might expect a significant therapeutic impact of interactions with animals is that of human affective disorders such as autism and schizophrenia where social and emotional interaction abilities with other humans can often be very seriously impaired. Indeed, there are a number of small case studies that do seem to support this conclusion although there seems to be a lack of larger scale, controlled studies. A recent reasonably detailed study on 7 institutionalised middle-aged schizophrenic patients reported significant improvements in social living skills scores over a 9 month period with weekly 50 min sessions with a therapy volunteer and their dog (Kovacs (2004)).

Allergies

Contrary to expectation a recent study has shown that children who grow up in families with cats and dogs as pets are less likely to develop common allergies. Children brought up in households with two or more dogs and cats were half as likely to develop common allergies (skin allergies and asthma). This is thought to be due to the endotoxins formed from the breakdown of bacteria in the animal's mouths making the patterns of our immune responses more effective.

Cognitive enhancement in mentally retarded individuals

An area where one might not perhaps expect to see advantages of interactions with companion animals is that of learning of cognitive skills. However, here again where correct performance of learning tasks is rewarded simply through being allowed to feed or stroke or interact positively with an animal this can significantly improve learning speed in both normal and mentally retarded individuals.

Postural control, co-ordination and balance

For individuals with physical disabilities affecting their control of movement, co-ordination and balance, therapeutic horseback riding (called hippotherapy) has been shown to be highly beneficial. Hippotherapy has also been shown to improve feelings of self-worth and power in individuals freed from the confines of their wheel chairs. Horses are also now used in psychotherapy to improve self-concept, self-confidence and social competence (Burgon, 2003).

Visual impairment

We are all very familiar with the huge benefits that trained guide dogs can bring to the blind. The close dependent relationships that such individuals have on such animals that are so important to their mobility and quality of life also has benefits for dealing with the psychological aspects of such a disability.

Prisons

Disciplinary problems with inmates in some US prisons have been reported to be reduced where they have routine access to pets.

How can pets/companion animals have these effects on us?

This is both an easy and a difficult question to answer. Easy in the sense that pets provide us with a source of pleasure, distract us from things that are stressing us and bring us out of ourselves, provide us with a source of social, emotional and tactile interactions at the simplest and least demanding level. They also appear to need us to be there for them and don't answer back when we use them as sounding boards for trying to solve our problems. Difficult because they are not substitutes for other humans and we all know deep down that in reality they can only provide limited social and emotional support – so why can't we get these things more effectively from other humans?

For individuals with affective disorders which give them significant problems with being motivated to seek social contact, and/or in responding appropriately socially or emotionally to others when they do try, then the simplicity of interactions with animals has clear advantages. The consequences of misinterpreting social and emotional signals with pets are also fairly minor and emotional feedback that companion animals can give from just simple gestures such as stroking and feeding provide a powerful motivation to engage with them. For disabled individuals the fact that animals like dogs and cats are seemingly completely oblivious to even the most severe physical defects is also a considerable advantage since this is something that other humans can find very difficult to deal with.

However, for the majority of us one would have thought that family and friends should be able to provide for us all, and more, of what even the most interactive companion animal could. Nevertheless, this conclusion

seems in many cases to be wrong and arguably as human society becomes increasingly demanding on each of us emotionally and psychologically our need for close contact with companion animals will increase.

There are those of course who consider that there is far more going on than this and that other animals are capable of influencing us in mysterious ways that are yet to be revealed by science. Claims of the presence of telepathic powers that dogs and cats may have in relation to communication with their owners and what impact these undefined communication sources might have on us are made frequently. However, the only species where claims of the potential physical impact of communication between humans and other species have some credible basis to date involve cetaceans such as dolphins.

Dolphin assisted therapy (DAT)

Of all the forms of animal assisted therapy a special place appears to have been assigned to dolphins and perhaps other cetaceans. Of course even if it does prove to be the case that dolphins can have profound therapeutic effects on children or adults with mental, emotional or social disorders any thought of breeding large numbers of such animals in captivity to make such treatment widely available is clearly unacceptable. The issue at this point is simply whether there is any scientific support for the beneficial claims that are made. If there is, then the next question is what are the dolphins doing that is having this effect and can we create it artificially?

Although one might consider that the fantastic experience of swimming and interacting with such an attractive animal combined with knowledge of their almost mystical reputation might be the key therapeutic factor this seems unlikely. For many who seem to benefit from the therapy the experience is, at least initially, quite a fearful one. Dolphins are large animals and could inflict significant damage on a human. Also many individuals who benefit from dolphin therapy are children who know little or nothing about their attraction to others or their attributes.

Of the remarkable claims made for the effects of dolphins on humans their keen interest in pregnant women, apparent ability to detect and focus attention on specific injuries and to alter the electrical activity of our brain would seem to demand some explanation. In relation to brain EEG patterns dolphin interactions have been reported to reduce the dominant frequencies from around 14-16Hz (Beta) to 6-8Hz (alpha/theta). This would seem to indicate a relaxed but attentive state. The interactions also promote increased synchronisation between the electrical activities of the two brain hemispheres. What might be causing this?

Dolphins will often direct their heads towards injured body parts or underneath the back of the head of a human floating on their back. This coupled with the fact that one of their key forms of navigating and communication involve the use of ultrasonic clicks at around 120KHz has led to the hypothesis that their therapeutic effects may be the result of this ability to produce directed ultrasound. Imaging forms of ultrasound are at low intensity and it is possible that the dolphins can use their object detection and identification ultrasound to detect the presence of a foetus in a pregnant woman or perhaps even body organs such as the brain and heart. However, while remarkable this would simply be a sophisticated non-invasive example of biological imaging with little potential for provoking physical changes in tissue.

At higher intensities, ultrasound has the potential to disrupt cell membranes and promote altered chemical release in the body. In humans it is used, for example, in the treatment of musculoskeletal disorders. This process is usually referred to as sonophoresis. However, benefits require multiple treatments that amount to quite long periods of exposure. A recent study on dolphins interacting with humans found that while their ultrasound intensities could just reach the required level the animals needed to be very close to a human (<1 m) for this intensity to be achieved and that the dolphins did not spend sufficient time close enough to

individuals even in repeated therapy sessions for physical effects to be expected to occur.

In terms of the influence that dolphins can have on human brain activity another suggested possibility is that a piezoelectric effect is created by ultrasound resonating with the bones of the cranium causing irritation of the brain. However, human swimmers rarely have significant amounts of their skull submerged so this seems unlikely too.

Overall therefore I tend to agree with conclusions made by Brensing et al. (2003) that the physical and therapeutic effects of dolphins on humans probably reside more in perception of their gentle and attentive behaviour towards us, possibly interacting with the sensory effects of an aquatic environment (although the latter is unable to evoke the same kinds of changes in the absence of the dolphins).

Robot therapists and virtual pets

While some humans are seemingly becoming as, or even more, interactive with their computers and electronic gaming systems than they are with either other humans or animals, and these devices can be both motivational and used effectively as learning aids, the one key missing component is some kind of genuine emotional response such as affection. Virtual pet software or simple talking electronic devices can be programmed to use emotional language and concepts but this is nothing like the feel of a contented cat, or a dog resting its head on your lap or licking your face or hands. So even though advances in robotic engineering may soon be able to give us electromechanical dogs and cats these are unlikely to prove as successful as the real thing. This does not stop the industry trying however, as can be seen with the Sony dog.

Designing new species: Out with the old and in with the new?

How then could humans design new living species to suit our needs? We can of course continue to utilise selective breeding strategies or simply rely on natural selection to evolve new species that are better adapted to human needs and human environments. There are also transgenesis approaches that can be used to incorporate specific features of one species into another. However, there are at least four other potentially controversial ways of creating new species that may not be so far off from being removed from the realms of science fiction.

The first and simplest method involves finding the precise environmental conditions that suit the natural evolution of the chemical building blocks of life and seeing what develops. A second approach could be to find a way to combine two separate species through the production of hybrid chimeras that were not sterile but capable of reproduction. A third approach would be the creation of a totally new species through the design of novel chromosome and gene combinations based on existing principles. A final fourth approach would be to do the same thing but using either a totally new synthetic biological replication mechanism or one that combines existing with novel synthetic processes. The last two possibilities make an important and highly controversial assumption, namely that we, as humans, have the ability to create life simply by assembling the appropriate organisation of existing or novel chemical building blocks.

This all sounds like something from Mary Shelley's *Frankenstein* and the realms of science fiction, fantasy and Hollywood films, but many scientists would probably lay significant odds to some or all of these things being possible through scientific advances during the course of this current century. Before you think that by saying this I mean beyond the lifetime of most of us, I should add that some of the enabling building blocks for these possibilities may well be established before the end of the current decade!

Defining life

Just what we consider as defining a living thing can be quite variable and most of us might want to make the case that simple organisms such as bacteria or viruses are qualitatively different from animals and even plants. Indeed, one of the motivations behind trying to recreate life is to be able to define it more accurately. From a biological perspective at least, and when things are reduced to their simplest level, a cell that is part of a living organism is self-contained (i.e. has some kind of semi-permeable structural membrane), requires and utilises energy (so it can function independently and grow), is capable of some form of replication (i.e. cells can divide in a way that they pass on the information contained in their genetic blueprint to all new cells) and can adapt to altered environments (by altered control of gene transcription for example). In a nutshell this is summarised by containment, metabolism and heredity being considered the basic components of cells that comprise a living organism. Most would add to that the ability to show evolutionary adaptation in Darwinian terms.

This pragmatic definition denies any idea of dualism which has often pervaded religion and philosophy – the idea that there is some form of requirement for a life force over and above the mere physical components of a living being. The same dualism has often been applied to the idea of a mind that is somehow distinct from the brain. Even Mary Shelley's Frankenstein had to be exposed to freakish environmental forces of massive electrical energy for him to become alive.

Chemical soup

Defining the necessary environmental and chemical conditions for evolving life forms has always been of considerable interest and could help us predict the extent to which life forms have evolved in other parts of the Universe. Since such an approach, even if successful, would take a very long time to recreate a life form I will not give it much consideration here other than to say that it does seem to be possible to recreate conditions where amino acids essential to living organisms, such as glycine, are generated spontaneously. This is a very long way from the creation of life however.

Mixing species

The phenomenon of speciation effectively isolates different species of life forms from combining their genes and creating functional chimeras which would represent a totally new species. This is not to say that anyone would really want to do this but one might see circumstances where combining the advantages of two different species into a single new one might be considered. Nature has provided two lines of defence to prevent this from happening. In the first place individuals from different species rarely show any form of sexual attraction towards members of other species. With mammals and birds this may be largely a by-product of parental influences creating an attraction blueprint (Kendrick et al, 1998). However, even where cross-species matings do occur and genetic similarities are sufficient for viable offspring to be produced these are invariably sterile. The classic example is a mule produced by a horse mating with a donkey.

Scientists have been trying to establish for some time what the key genetic changes are that effectively isolate one species from another reproductively. While there are likely to be multiple factors involved it appears that one of the key ones may be the different arrangements of chromosomes in different species. Experiments with yeast have revealed that the sterility issue at least can potentially be overcome by realigning the chromosomes in different species of yeast. This work has been carried out by Professor Steven Oliver's group at the University of Manchester (Deineri et al, 2003). It should be possible to realign chromosomes in the same way in genetically similar, but distinct, animal species. So somewhere down the line, and accepting that there are likely to be a number of other genetic differences contributing to the reproductive isolation of specific species, it may be possible to produce a new species with the combined traits of two different ones.

Building from a blueprint for life

The idea of producing life using a bottom up approach of stripping down a simple living organism to its basics and then trying to reproduce it artificially has been proposed in particular by Craig Venter in the USA (of human genome sequencing fame while working for Celera). In principle the idea is quite compelling. First take a very simple species, such as a bacterium, with a small genome and keep taking away genes until you reach the point where it ceases to function normally as a living organism. To do this they used the bacterium *Mycoplasma genitalium* which lives in the human genital tract and has only 517 genes (compared with around 30,000 in humans) by systematically inactivating genes they were able to produce a version of this bacterium that could function with 250-300 genes.

Craig Venter is currently collaborating with the Nobel laureate Hamilton Smith to reproduce this cut down version of the bacterium artificially from its component parts to establish whether a simple life form can, in effect, be created this way. The major stumbling block is likely to be in recreating the necessary interactions between the component parts. If for example one uses a simple analogy of some kind of motor to illustrate this point, then imagine you are given the component parts and an instruction manual which details how they should fit together you might expect to be able to build a functioning motor. However, if the manual was lacking precise details in a few places and some parts were not assembled in the right place, or alternatively perhaps a few of the parts were missing then when you built the motor it might not work at all. It might then take some time to sort out what was missing or in the wrong place

Nevertheless, there is some degree of confidence that this approach will work and that if it does this will open the door to redesigning the simple genome of this species to allow it to perform functions that may be of direct use to humans.

The Los Alamos Bug

A more radical approach, which to some extent avoids a few of the potential pitfalls of trying to guess how existing living things by recreating them, is to design new life from scratch. A number of groups are trying this more bottom up approach to creating life that while still guided by existing life forms is effectively novel and completely artificial. For example a group at the Rockefeller University in the USA have managed to create small synthetic vesicles that are able to express genes in a simple cell. They were able to visualise the success of this attempt by having the gene transcribe a fluorescent protein taken from a jelly fish which made the vesicles become green (Noireaux and Libchaber – 2004).

Meanwhile back in Los Alamos, the birthplace of the atomic bomb, Steen Rasmussen and Norman Packard and their colleagues have been awarded a \$5 million grant to create a completely new life form. The blueprint for this has been described in detail by Bob Holmes in a recent article in *New Scientist* (Holmes, 2005). In essence this describes a series of steps using synthetic molecules which should enable living cells to be created which have containment (external permeable membrane), are capable of replication and passing on hereditary information and to metabolise nutrients, grow and divide. It even uses a novel form of replicative process using short stretches of peptide nucleic acid (PNA) rather than DNA although there are a number of similarities. One major difference is that the artificial cells will be oil rather than water based. They will, in effect, be an oily droplet of fatty acids. In brief the following strategies have been adopted to fulfil the criteria for life:

Containment

The cells are suspended in a watery solution in a test-tube. The fatty acids used to make up the cell have a head that is negatively charged and attracted to water and a tail that is positively charged and therefore hydrophobic. The molecules will therefore cluster together in a watery medium with their heads facing outwards to make a permeable containment membrane and anchored in place by their tails which face inwards trying to avoid the water.

Heredity

The short stretches of peptide nucleic acid that will be used are like DNA in that they have two intertwining strands made up of the classic A, T, C and G nucleotides (with A's matched to T's and C's to G's across the strands). The strands do not have a charge, dissolve in fat and naturally sink down towards the centre of the cell where they therefore dissolve (in a temperature dependent manner) and unzip to form single stranded PNA. The bases when exposed have a slight negative charge and so migrate to the membrane surface of the cell and can then link with "nutrient" single stranded PNAs (each around half the size of the total genome) present in the watery medium outside the cell. When two of these fuse to the bases of the single stranded PNA the resultant double stranded PNA loses its charge and sinks down into the cell and then the whole process starts again. This is therefore a very simple and controllable form of replication.

Metabolism

The cells of this "Bug" will be fed with fatty acid precursors introduced into the external watery medium. These have photosensitive molecules attached to their charged head ends but which cover the charged molecules. In this way the nutrient fatty acids are fat soluble and sink to the middle of the cell. However when exposed to light this removes the photosensitive cover on the head of the nutrient, it becomes attracted to water, travels to the surface and thereby increases the size of the cell. When enough of the nutrient molecules have done this the membrane reaches a critical size and when surface tension can no longer contain it, the whole cell droplet splits to form two cells. So we have nutrient stimulated cell growth and division. The bug will also have inactive photosensitive versions of PNA which can become activated in response to light and thereby increase transcriptional activity in association with the growth of the cell. The genetic material of the PNA is also designed to remove electrons from the detached photosensitive molecules so that they cannot reattach and deactivate the PNA itself or stop the nutrient fatty acids from promoting growth.

Evolution

In theory at least with all the cells together in a test-tube natural selection should favour the PNA base sequences that pair up and spit most quickly and are most effective at preventing photosensitive molecules from reattaching themselves to the PNA or fatty acids.

The kind of cells being designed here would be totally dependent upon the support of substances introduced into their artificial medium and this would make them incapable of independent survival. However there are other groups who are working on methods for making such an organism capable of monitoring its own functions and of precisely controlling its own transcriptional and metabolic activity.

This is clearly a long term project but it would be a remarkable juxtaposition if Los Alamos was the scene for the first demonstration of the being able to create life after its previous use for creating a force that was a potent destroyer of it!

What could this lead to?

So yes let's be prudent and admit that the kinds of approaches outlined above for creating any form of complex life may still be a long way off. The point, however, is now more about "when" rather than "if". It is likely that some simple form of artificially constructed life will have been produced by the end of the current decade. Scaling up to larger scale organisms capable of self-repair, evolutionary adaptation and self-sustaining in a normal external environment may take until the middle of the century or longer. Chromosomal manipulations may also allow the production of reproductively viable cross-species chimeras by this time, at least involving species that have close genetic similarities. We might of course choose to

ban, or limit in some way, the exploitation of this technology but that should not prevent consideration of what we might actually do with it if it was available?

If we able to design and create new life forms we would be likely to use them to help deal with specific human and environmental problems. On the plus side we could create micro-organisms to help with food and energy production, waste disposal and pollution control. We could design organisms that could be introduced into the human body to target disease or even rebuild damaged tissue. However, it will be a two edged sword. New life forms could also be produced for the purpose of biological warfare, and just how far could we go in designing the perfect companion animal bearing in mind our growing dependence upon them and the extremes some individuals are already prepared to go in relation to use of selective breeding and cloning?"

One might argue for example that the creation of simple new life forms could help replace our use of more complex, sentient ones for food production and even some routine aspects of biomedical research. Such an idea would clearly present something of an ethical dilemma.

An even more complex ambition could be to produce other companion animal species. Humans seem to have an increasing need for emotional and psychological support from simple but attentive and affectionate life forms. While animals like dogs and cats currently supply this for many, the large numbers of them that are abandoned and/or mistreated by their human caretakers show that they are not always the perfect solution. As I have argued already it is more that attentive, affectionate and playful nature of such species that really attract us. In spite of our finding the portrayal of highly intelligent, talking animals entertaining this simply makes them into human look alike and their resultant psychological and emotional complexity would make them lose many of the advantages they currently have. So if one had to consider what different or enhanced characteristics we might want a companion animal to have it might simply be more of the same and perhaps to live longer so we avoid bereavement issues.

Whatever we can theoretically or practically create, and whatever the moral and ethical concerns of society allow, there is little doubt that by the end of this century the numbers of naturally evolved species still viable on the planet will be in serious decline, particularly the larger mammals, birds and reptiles that require large habitats. To some extent this seems inevitable since humans are a continuously resource hungry species and our increasing utilisation of it will make it difficult for other species to exist. Even if some predictions of a stable or reduced global population number prove to be correct it seems likely that resource consumption per capita will continue to rise. We may truly be the Gods of the planet, able to create new life forms at will as well as to destroy them if we manage to avoid destroying ourselves first. This is also not to say, of course, that evolving Homo sapiens into a different species could ever be entirely excluded from any potential agenda.

© Professor Keith Kendrick, Gresham College, 7 April 2005

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