Synthetic biology

A public lecture given by Robert Anderson PhD
(Length: 31 pages and 36 slides)

N.B. Some facts and figures may have changed since the lecture was presented.

Slide 1

Technologies such as synthetic biology, genetic engineering and nanotechnology are linked and I can only hope to just scratch the surface in an effort to give a preview of these today.

Synthetic biology - or, to use its sexier acronym, SynBio - is mainly at the laboratory stage, nanotechnology[1] is not and genetic engineering has been around for some decades. Most public and even many in government are not aware of the meaning of these terms. Yet they will come to revolutionize our world as we know it.

Synthetic biology and nanotechnology are used to describe a new area of research that combines genetics and nanotechnology in order to design and build novel biological organisms and systems. We are now able to engineer viruses, make new ones or modify old ones. We can change bacteria in ways we could never conceive of doing previously.

In short, we can now truly play God. Which immediately begs an obvious question: Do we have the necessary morality to do so?

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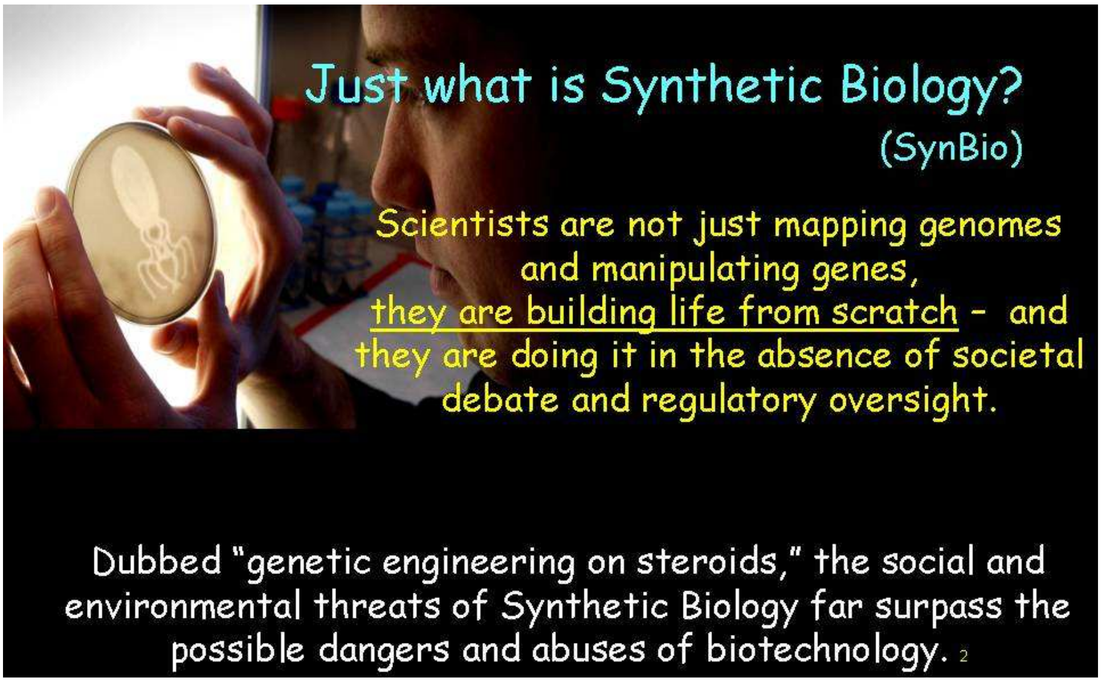
[1] See also lecture on "Nanotechnology"

Slide 2 - What is synthetic biology?



Synthetic biology is inspired by the convergence of nano-scale biology, computing and genetic engineering.[1] Using nothing larger than a laptop computer, we can publish gene sequence information and mail-order synthetic DNA.

What does this mean?

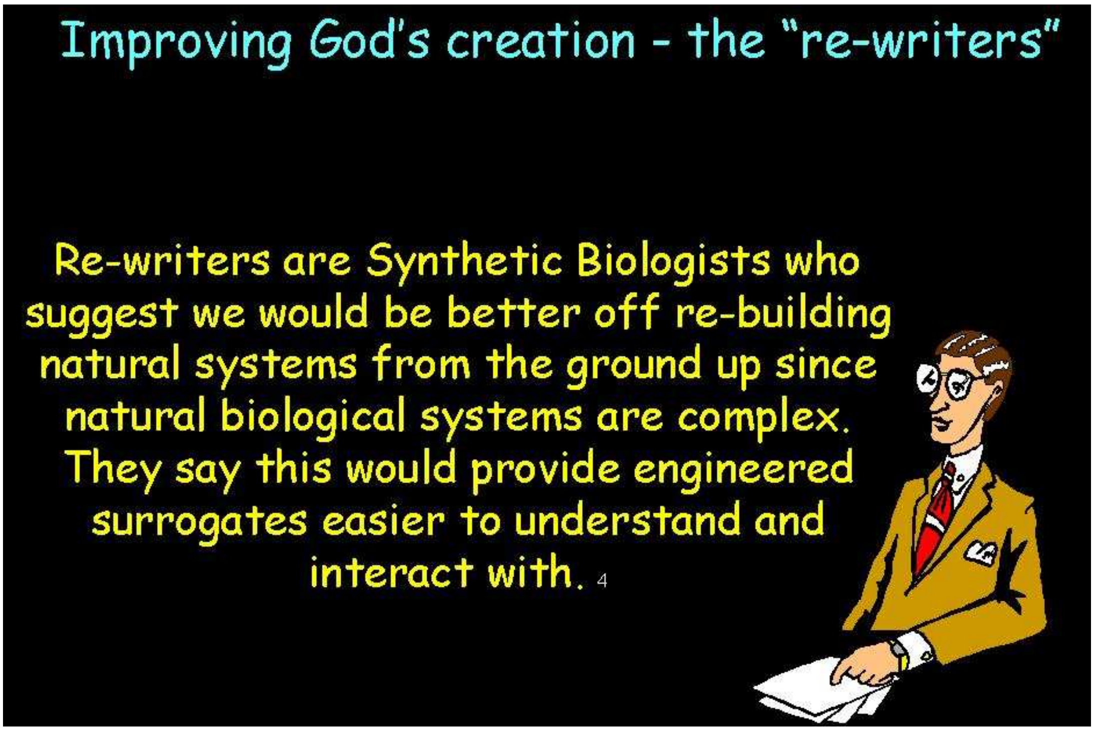
It means that almost anyone who has the right skills also has the potential to construct genes from scratch. This includes those of simple bacteria or lethal pathogens. Proponents claim that, in three to five years, simple bacterial genomes will be synthesised routinely. It will be no big deal to cobble together a designer genome, insert it into an empty bacterial cell and – hey presto – give birth to a living, self-replicating organism.

This is cause for some concern.

Man has always been an arrogant creature. (Notice I am careful not to include our women folk in this - my wife is in the audience.) But I would never have thought that remarks such as the following would have ever been voiced in the media.

[1] Synthetic biology has recently been called GE on E (as in ecstasy).

Slide 3 - Improving God’s creation.



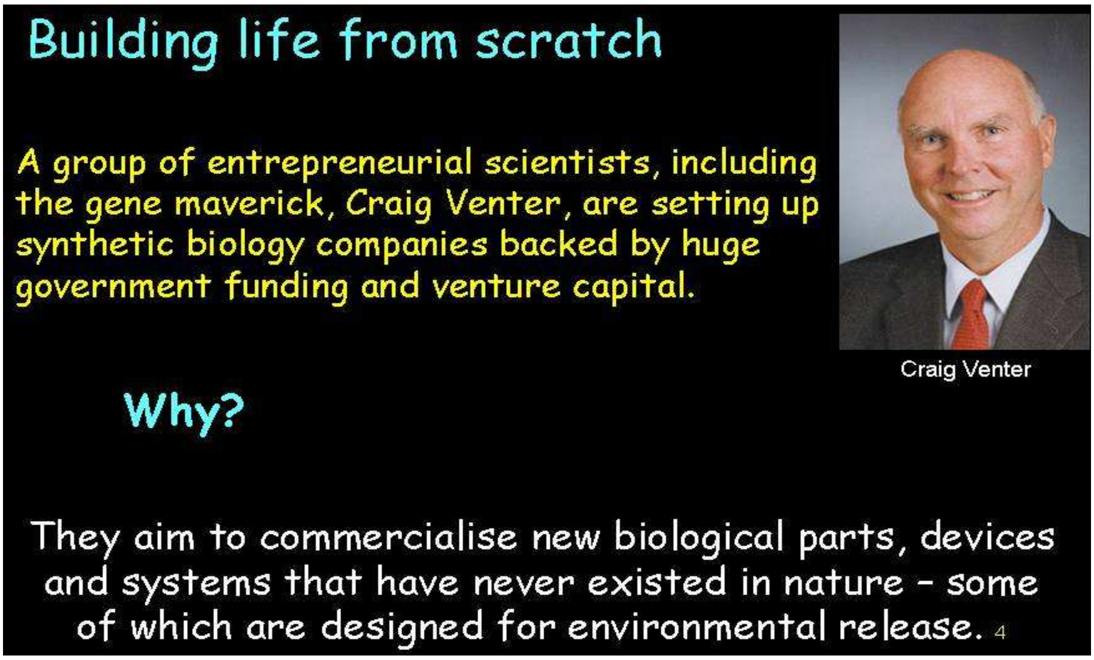
In 1978, a Nobel Prize in physiology and medicine was awarded to three scientists for the discovery of restriction enzymes and their application to problems of molecular genetics.

What is a restriction enzyme? A restriction enzyme is used like a pair of scissors to cut up bits of DNA. Another enzyme - DNA ligase - can rejoin them like “glue.” The discovery of these “cut and paste” enzymes made genetic engineering possible.

In an editorial comment in the *Journal of Genetics* one scientist wrote: “The work on restriction enzymes not only permits us to easily construct recombinant DNA molecules and to analyse individual genes, but has also led us into the new era of synthetic biology where not only existing genes are analysed but also new gene arrangements can be constructed and evaluated."

What is he saying? He is talking about creating *new* life-forms.

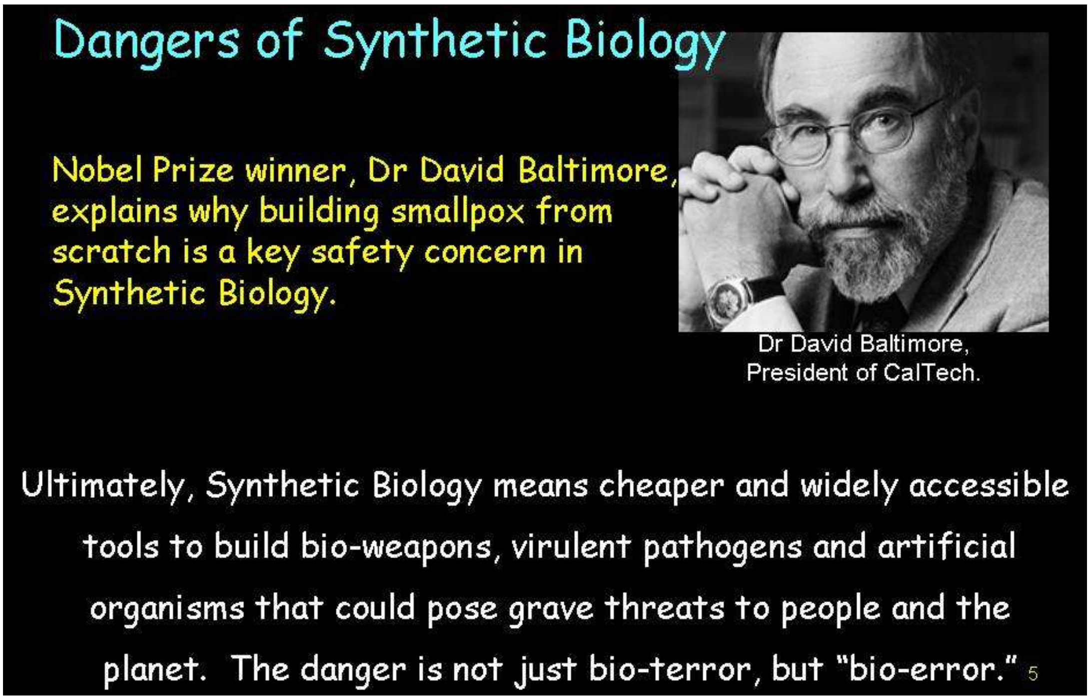
Slide 4 - Building life



Being able to design and build new life forms that can perform useful functions brings exciting promise. Scientists now have the ability to synthesize entire strings of DNA and put together complex molecular machinery. I will show you some of these shortly.

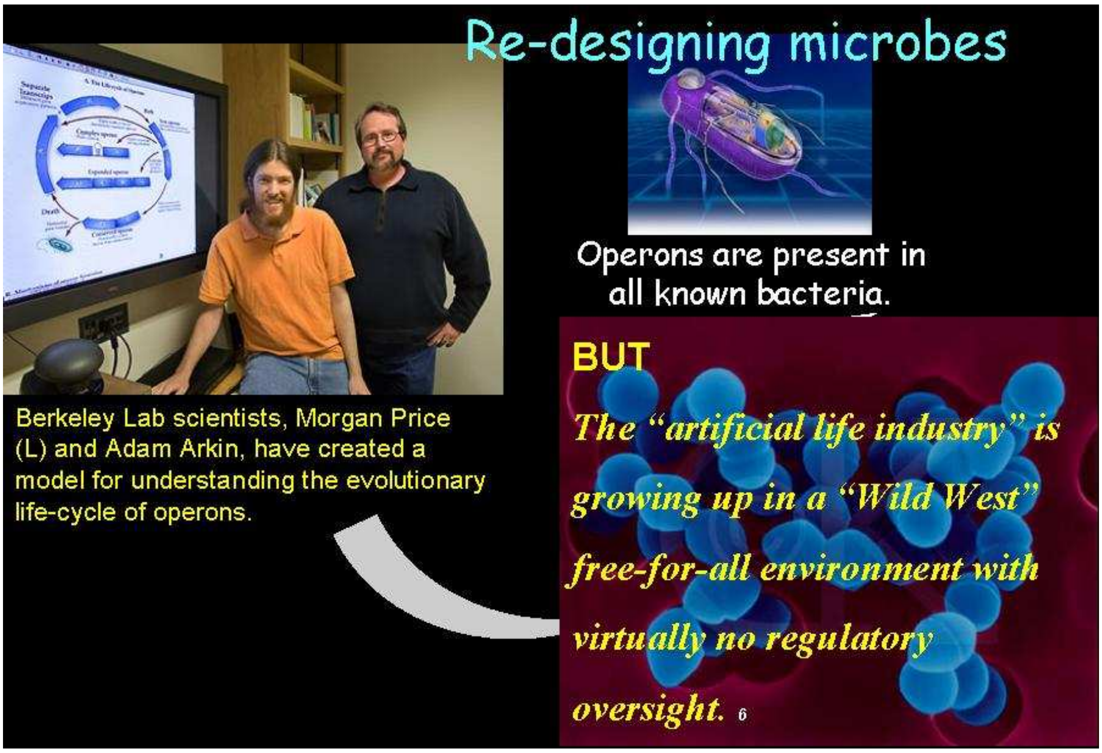
But that ability has raised some troubling questions. Terrorists or dictators could also recreate viruses such as smallpox, or engineer a virus even more deadly than avian flu. Professor David Baltimore, a leader in the field, agrees this is a real danger.

Slide 5



The other danger, allied to this, is the new ability to modifying bacteria.

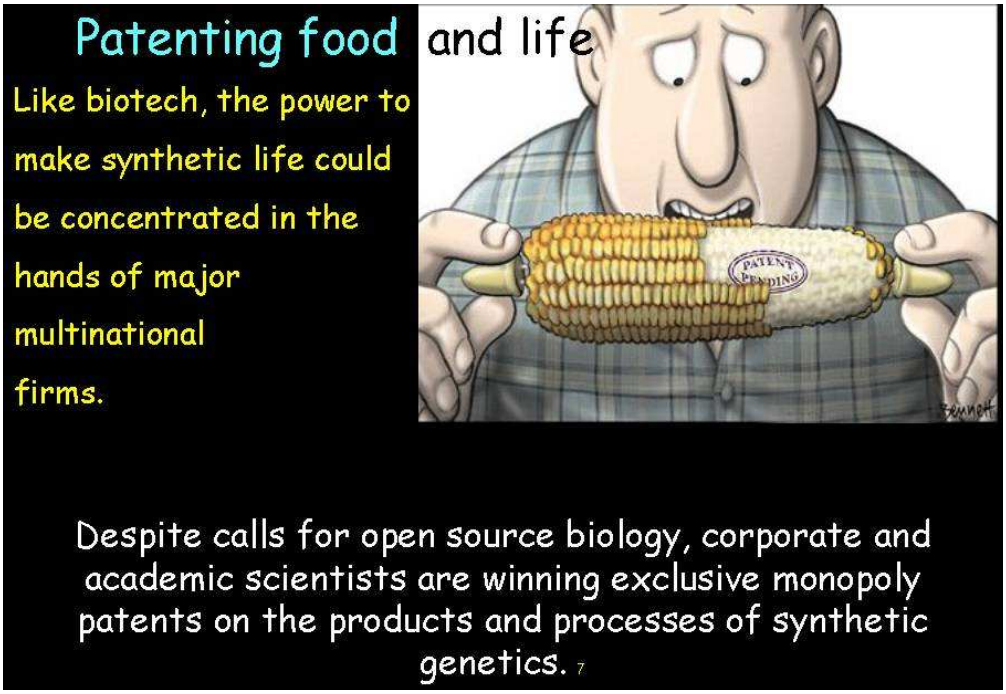
Slide 6 – Operons



Understanding operons means that microbes can be genetically engineered to make specific products, such as new medicines. Emerging applications of synthetic biology such as this DO need to be examined for their security and safety.

Another growing problem are patent laws. We have seen how the patenting of food systems and life forms became common with biotechnology,[2] particularly genetic engineering technology. In synthetic biology it could be even worse.

Slide 7



[2] Biotechnology is often used when genetic engineering technology is the more correct wording. It has been estimated that genetic engineering technology represents about 3% of biotechnology developments.

As gene synthesis becomes cheaper and faster, it will become easier to synthesise a microbe than to find it in nature or retrieve it from a gene bank. The tools for synthesizing genes are widely accessible and growing fast.

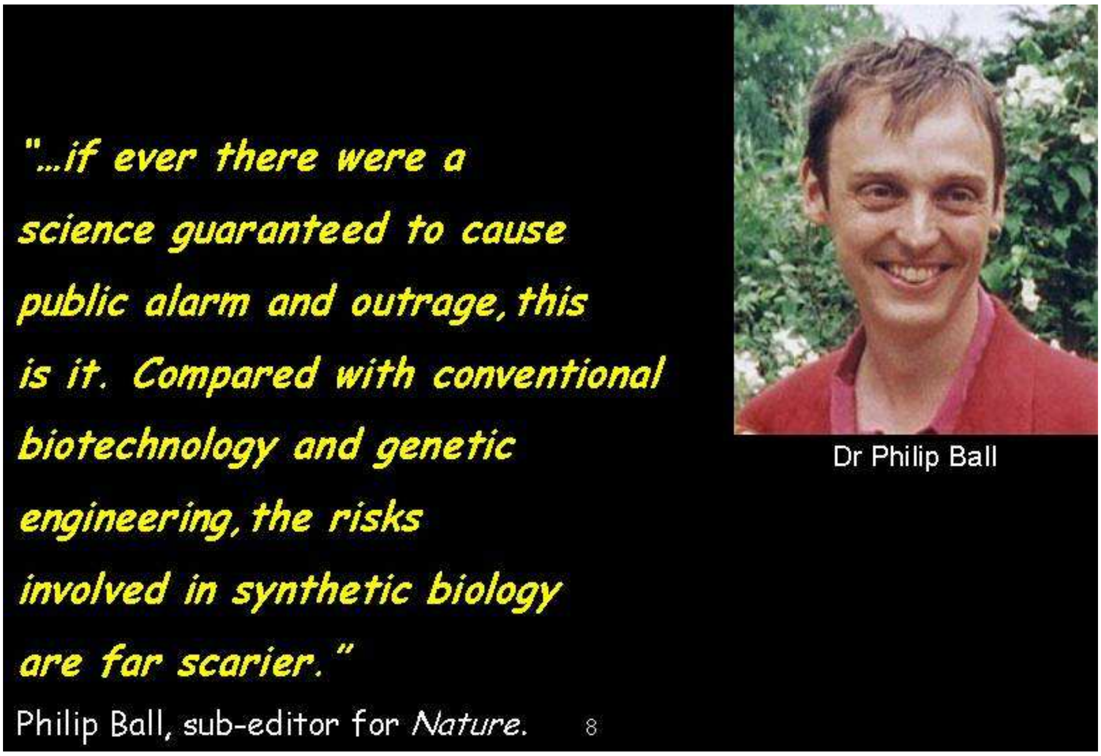
It is not adequate enough to regulate synthetic biology at the national level. Decisions must be considered in a global context, with broad participation from civil society. In keeping with the *precautionary principle*, there should be an immediate ban on environmental release of any created synthetic organisms until wide societal debate and strong regulations are in place.

There was an interesting letter sent to the *New York Times* recently. It was written by senior scientist, Rob Carlson, who is a synthetic biologist at the University of Washington. I quote to you:

"Genetic engineering techniques are abysmally primitive, akin to swapping random parts between random cars to produce a better car. With transgenics, genetic engineering was a cut and paste affair. Biotechnologists shuffled pieces of DNA between already existing species. By contrast, synthetic biologists are armed with the biological equivalent of a word processor. Using gene synthesisers, they write the 'sentences' of DNA code one 'letter' at a time. They can add new letters or combinations that have never previously existed in nature. They can rearrange the letters into new 'genetic networks,' and bundle them into an artificial casing to go forth and multiply. As attention switches from reading to writing genetic information, synthetic biologists can now snub their noses at nature's designs in favour of made-to order life-forms."

Dr Philip Ball, the sub-editor of the prestigious magazine, *Nature*, said this.

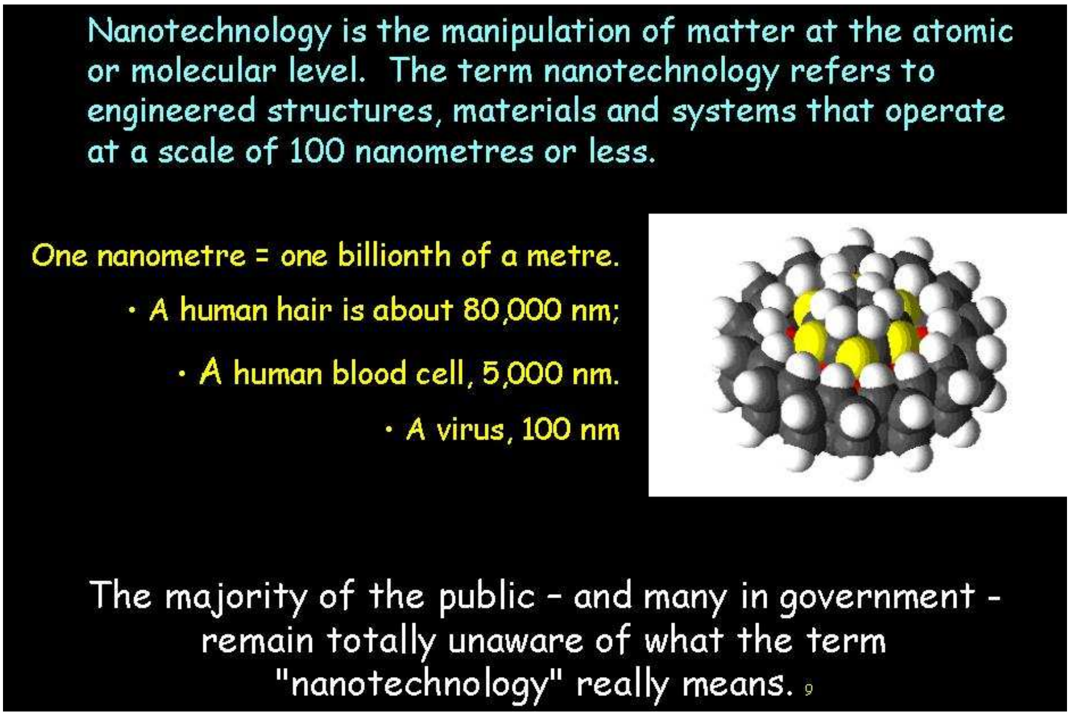
Slide 8



Millions of dollars of government and corporate funding are going into synthetic biology laboratories. Scientists from disciplines such as biotechnology and physics are manipulating matter on the *nano*-scale[1] of atoms and molecules. These sizes are very hard to contemplate so let me give you an indication here.

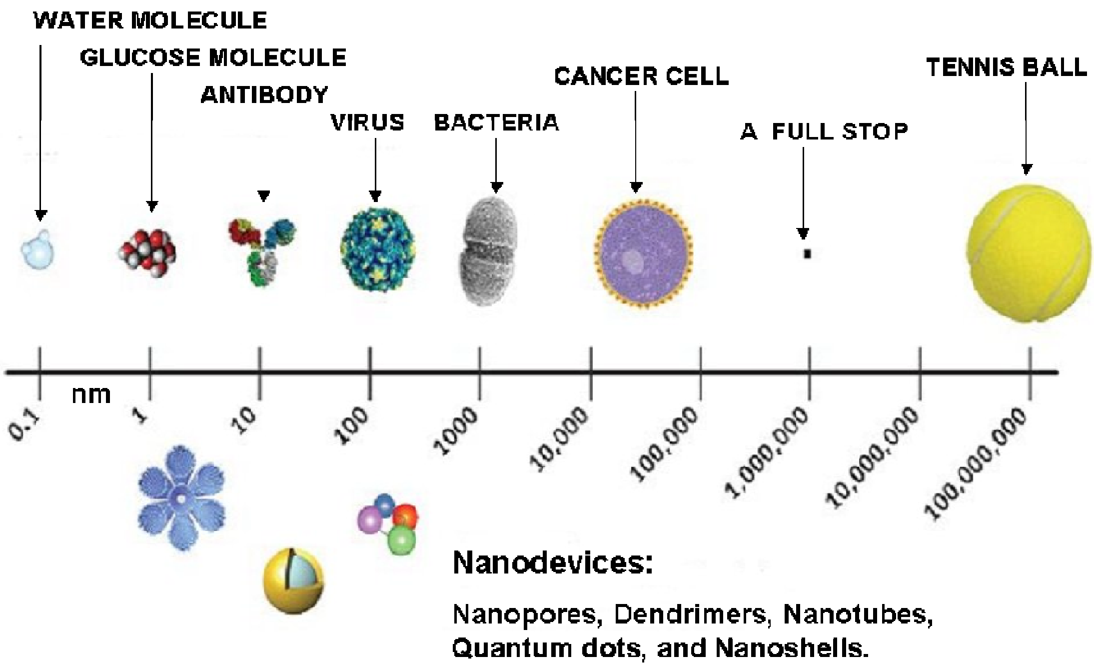
[1] See also lecture on "Nanotechnology"

Slide 9 - What is *nano*technology?



At this tiny scale, we can produce instruments small enough to work in the confines of the human body and there are many more wonderful applications on the horizon for this technology. It is easier if we look at a scale diagram to get some idea of the ultra microscopic world in which scientists now work.

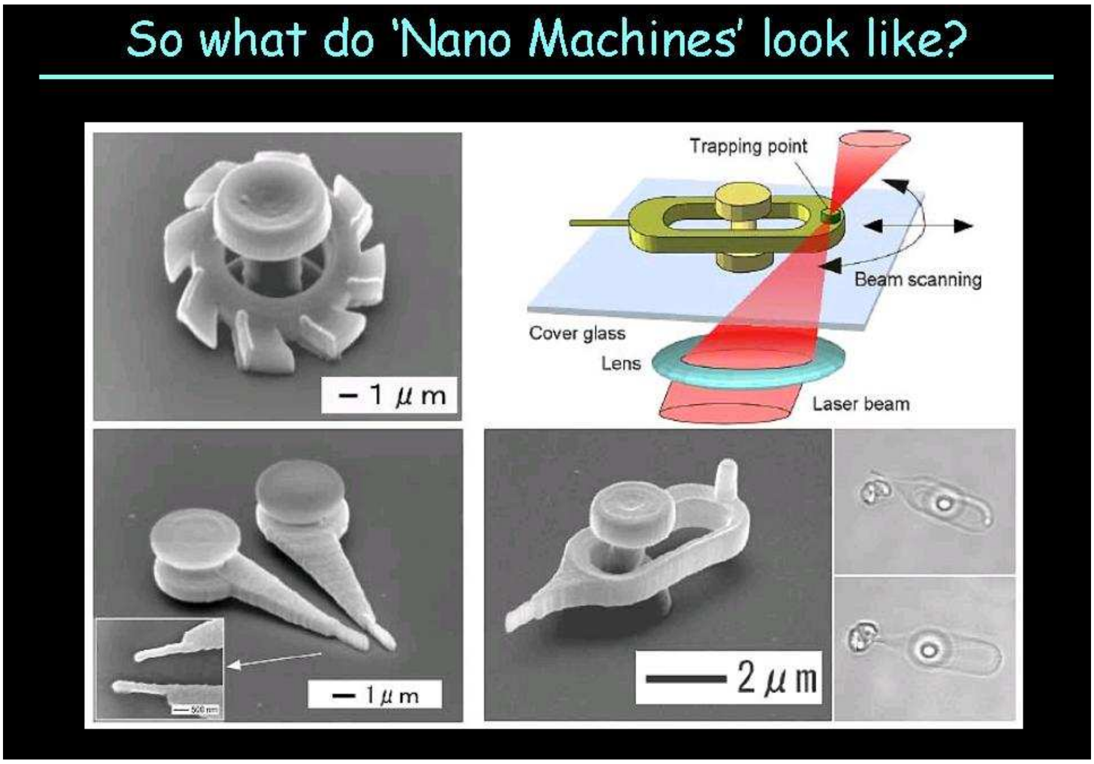
Slide 10



This is a whole new concept. These new technologies will revolutionise our world and society in a very profound way, much as the industrial revolution did.

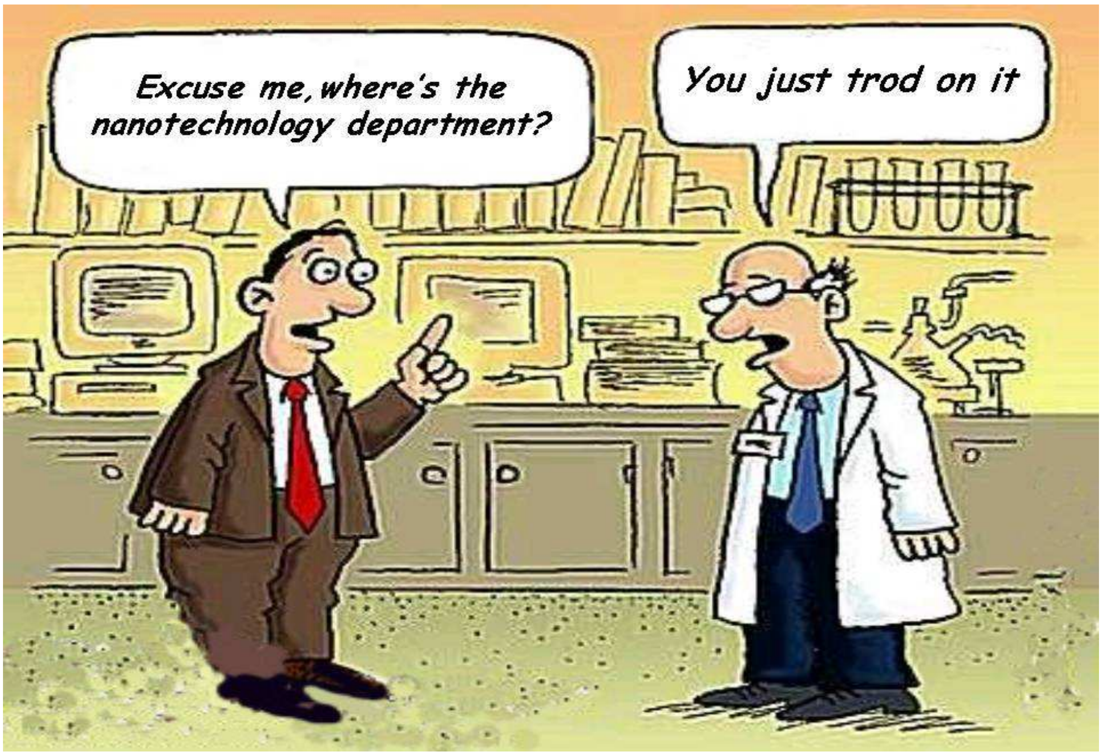
So what do nano machines look like?

Slide 11 - Nano machines



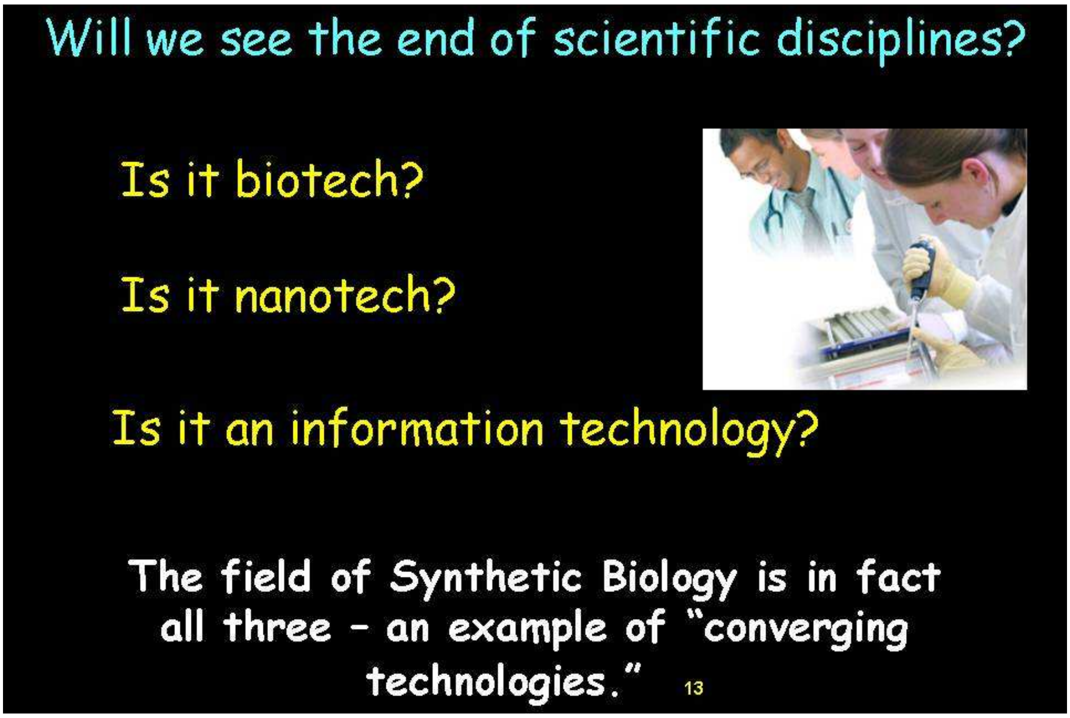
Using lasers and other technologies, nano-machines will be able to carry out enormously difficult tasks, to fit into areas where we have never been before: into blood capillaries, kidney cells and possibly even brain cells. We are talking here of a scale so small only an electron microscope would allow us to see it. We can probably illustrate this best for you with a cartoon…

Slide 12



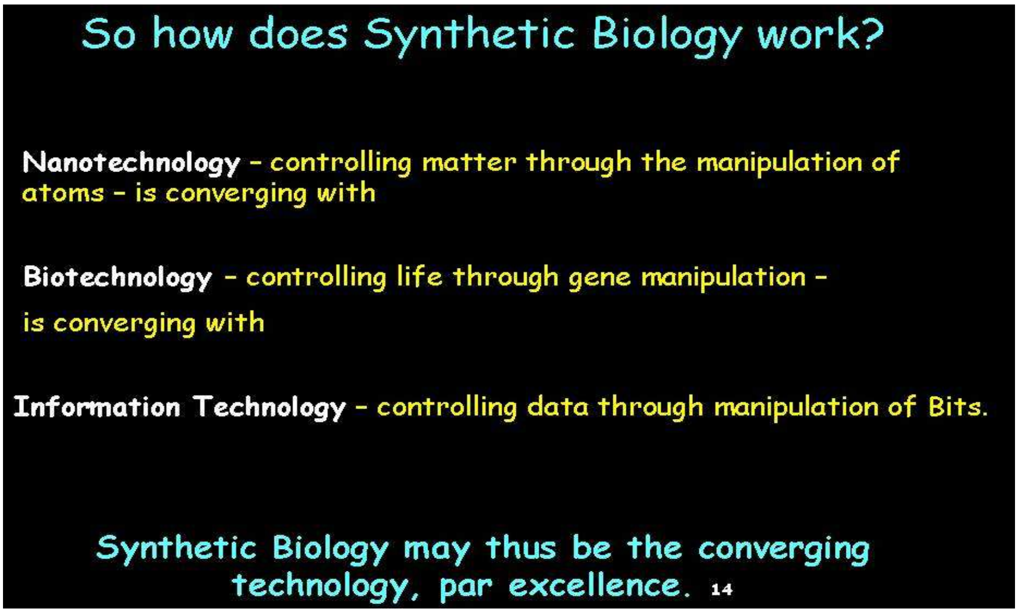
All joking aside, we are now seeing nanoparticles in our food and other products. And there is no regulation and no testing of these products.

Slide 13 – Nano sunscreen



As these scientific disciplines converge – nanotechnology, molecular manufacturing, and synthetic biology - they will radically transform our world and the people of the 21st century. Furthermore, nano-biology could mark the end of separate disciplines as we know them.

Slide 14

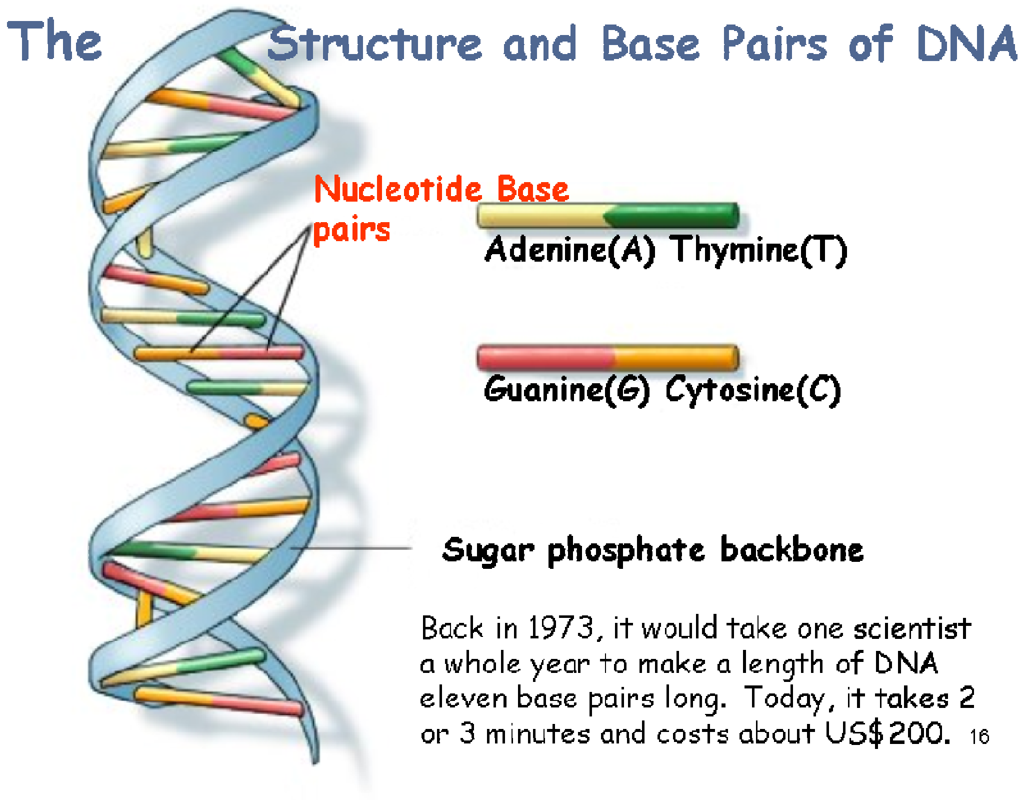


At the core of SynBio is a belief that all the parts of life can be made synthetically - that is, by chemistry. They can be engineered and assembled to produce working organisms. Born in the dot-com era, synthetic biology is often articulated using computing metaphors. Worldwide, governments and industry have enthusiastically embraced (and financed) the technological convergence at the nano-scale.

The US government is the loudest cheerleader for this convergence strategy. It refers to these new technologies as NBIC - an acronym derived from the technologies involved: nanotechnology, biotechnology and information technology.

Slide 15 – DNA

Synthetic biology refers to the design, fabrication and engineering of biological components and systems that do not exist in the natural world, and to the re-design, fabrication and engineering of existing biological systems. The basis of this new development is the manipulation of DNA - deoxyribonucleic acid - the molecule of life, and it may be helpful here to briefly revise the structure of the DNA molecule. As you will see on this slide, the nucleotide bases are represented by the letters A, G, C and T, and these form the spiralling ladder of the DNA molecule, the double helix. By arranging these four bases, scientists can now manufacture genes.



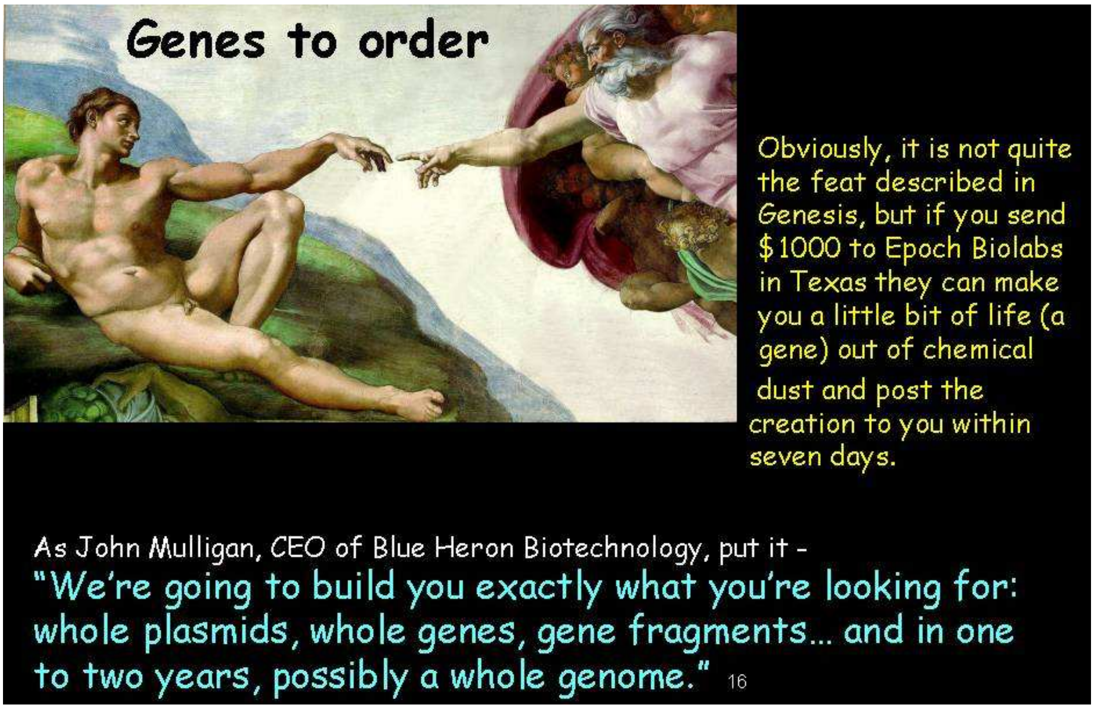
Across the globe, a plethora of gene synthesising companies have sprung up. They are building artificial life one chemical at a time. They then ship it, as small sections of DNA, to laboratories worldwide, and these laboratories are pushing the limits of what is possible in the SynBio field.

Admittedly, it still takes some fairly slow and complicated chemistry, but nevertheless it is now possible to assemble life.

There are at least 66 commercial gene synthesis companies currently operating and that number is growing. According to one industry estimate, the current market for gene synthesis is US$30-$40 million per year.

In other words, we have…

Slide 16 – Genesis



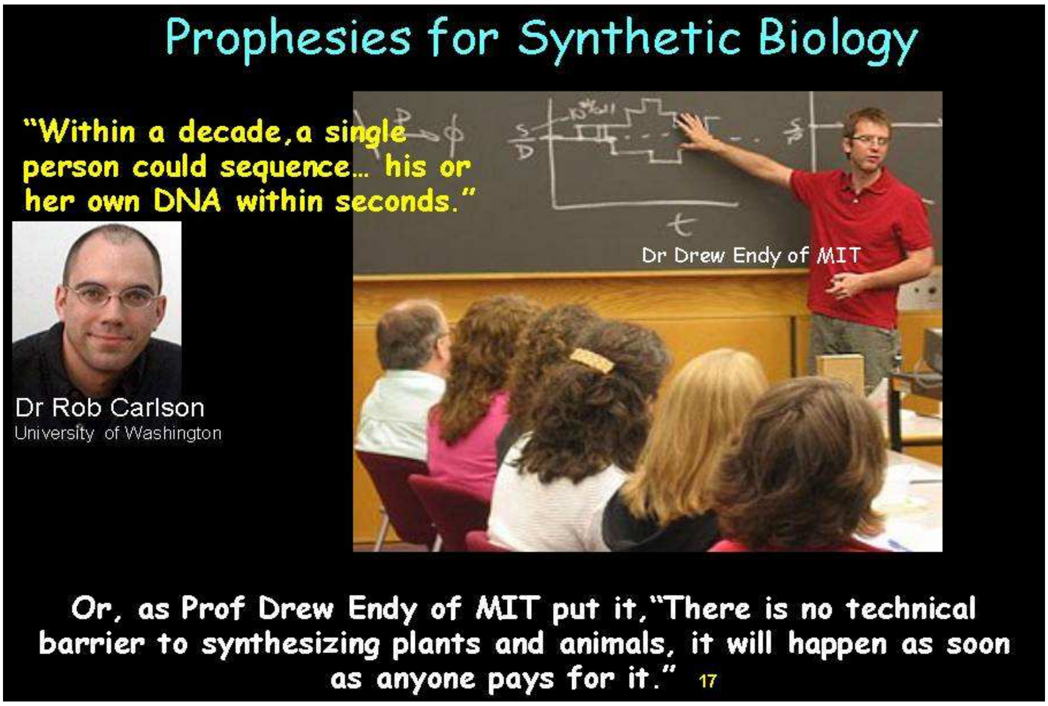
Some companies boast that there are no technical limits to the length of DNA they can produce. (I should add here, however, that most sequences are not error-free.)

Synthetic biologists predict that a million base-pair bacterial genomes will be constructed within the next two years. To give you a grasp of what this means, the common yeast genome is about 12 million base pairs long. This would take about 18 months to synthesise.

But - as more commercial gene-synthesis equipment becomes available - these synthesis times will continue to grow shorter.

There are some worrying prophesies on the horizon…

Slide 17 - Prophesies



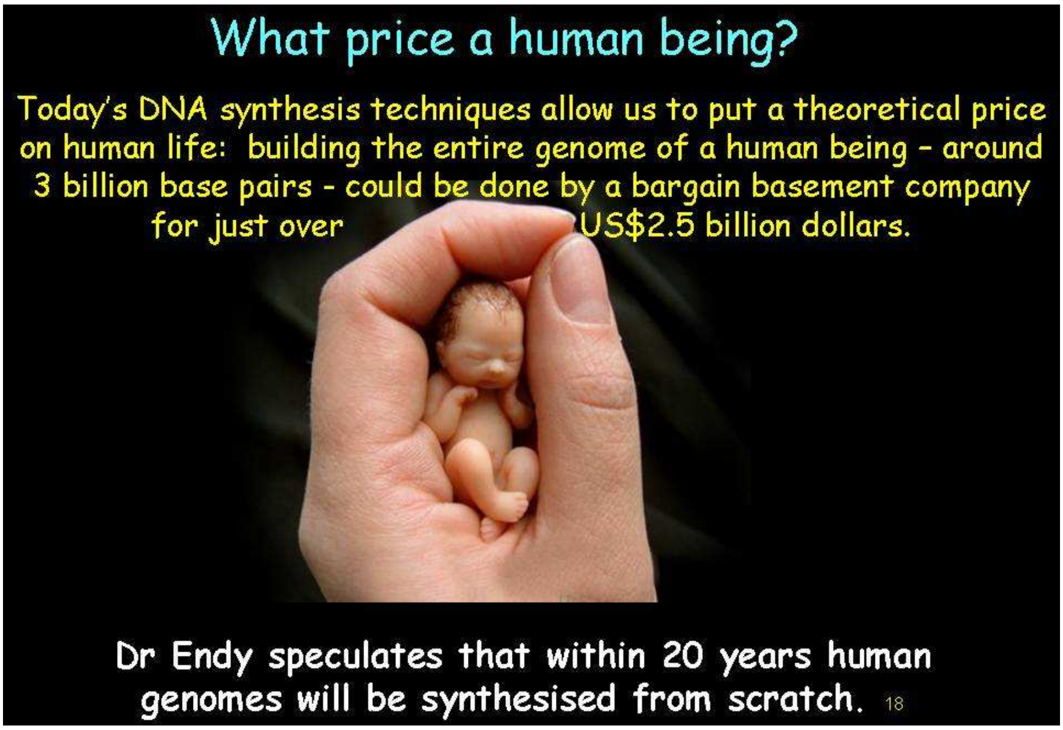
Professor Drew Endy maintains that do-it-yourself synthesisers could eventually be built using parts found in a hardware store. Good news, you might think … for countries bent on biowarfare.

DNA is getting pretty cheap to make. What does this mean to the ordinary consumer?

If you want to order a synthetic virus from Epoch Biolabs, they would charge you less than US$6000 to synthesise it. It would take them only three or four weeks to do this. A scientist colleague was offered such a service … in case he was too busy with other projects to do it himself.

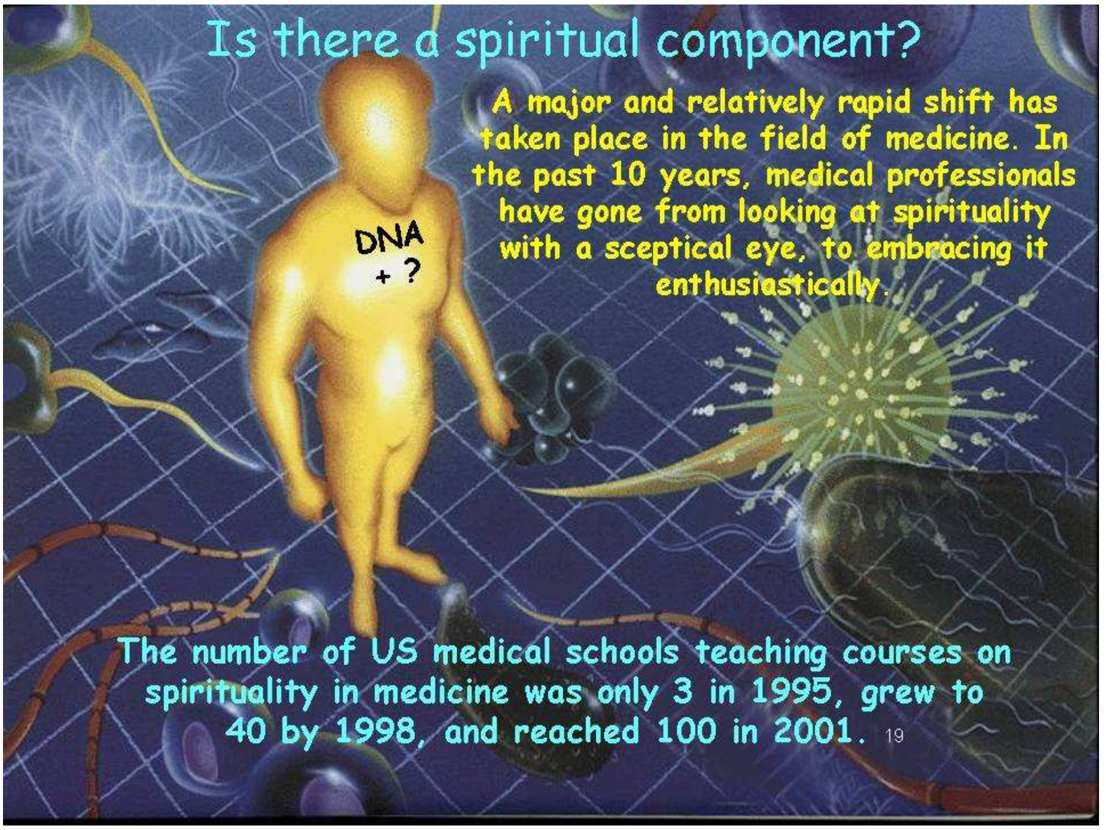
So what about the human organism?

Slide 18 - What price a human being?



Perhaps this may be so, but aren't we forgetting something here? We are not just a string of four letters. There is a spiritual component to all this. We are body, mind and spirit. Even medical science now recognises this.

Slide 19 - The spiritual component?



Cranking out DNA is pointless unless scientists know how to arrange it into meaningful code.

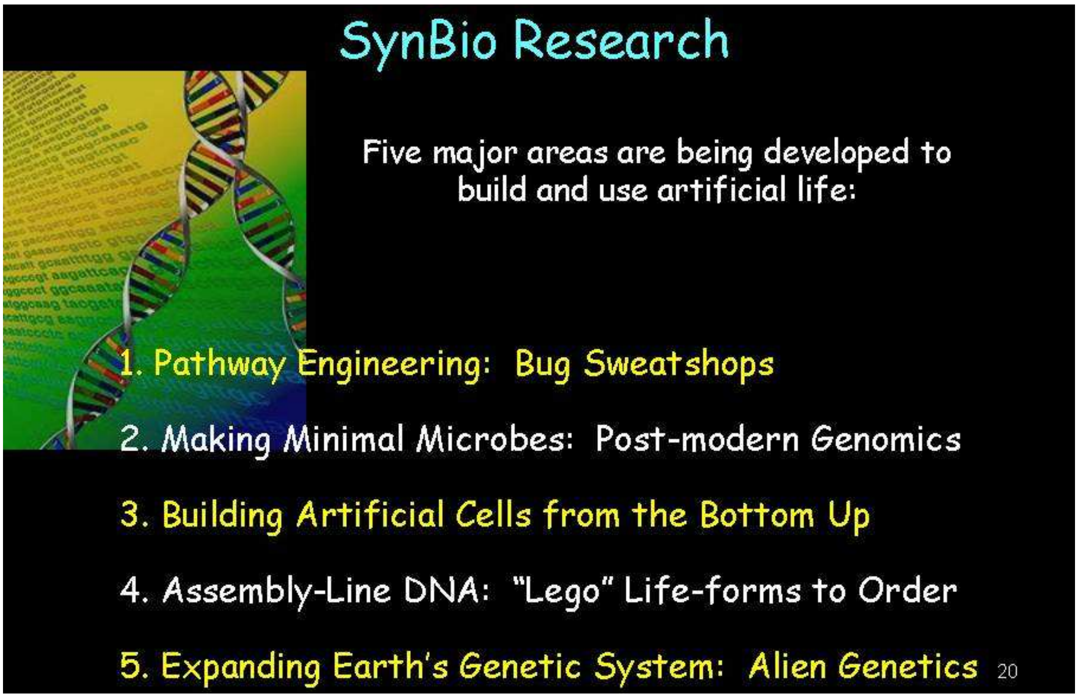
As I have said, in the popular understanding of genetics a gene is a length of DNA composed of base pairs. This is regarded as the smallest functional unit of genetic code which will instruct a cell to make proteins. In turn, those proteins carry out the tasks and processes within organisms that we understand as "life."

Francis Crick, co-discoverer of DNA's double-helix, put it cryptically. "DNA makes RNA, RNA makes proteins, and proteins make us."

Unfortunately, for our life-builders, the genetic code is not linear, nor is it that simple. In real life, genes co-operate in subtle and highly complex networks. The "Lego" model concept breaks down occasionally. Even so, there are five major project areas on the drawing board.

Slide 20 - Five areas

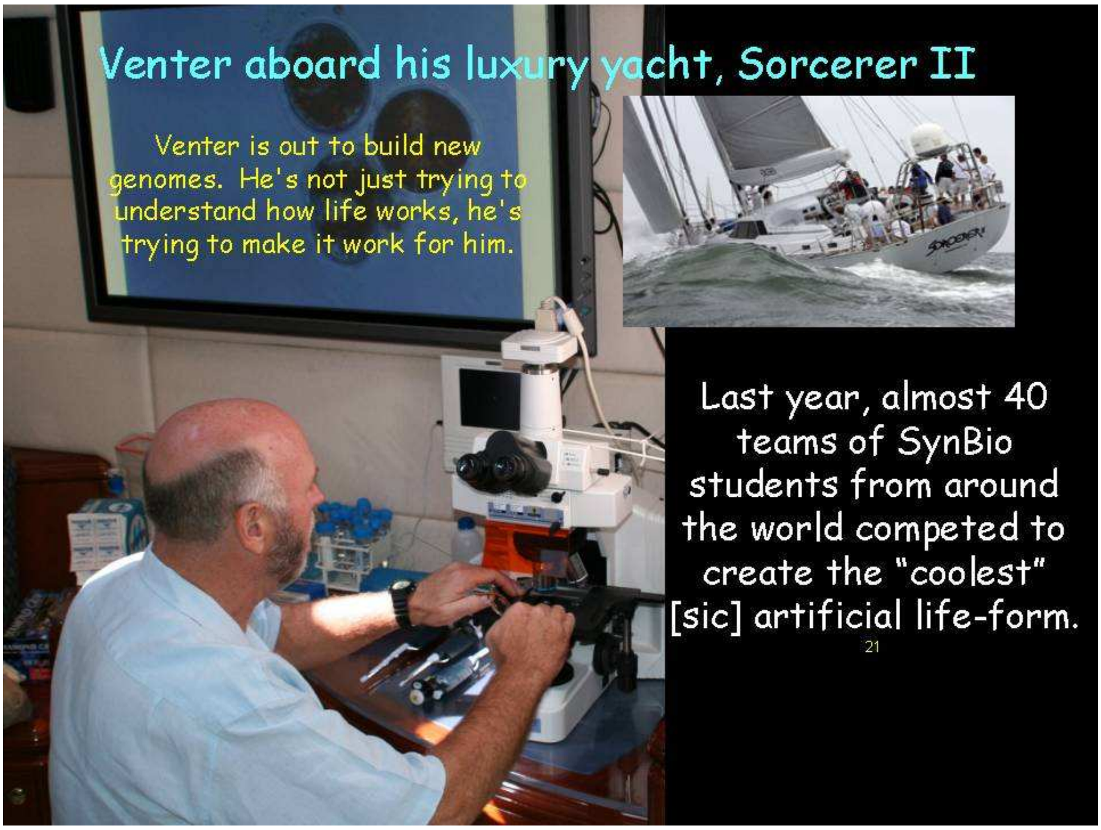
Mind-boggling applications such as these are now on track.



In the race to synthesise life, genomics magnate, Craig Venter, overshadows the rest. He is well-known as "biology's rogue scientist." Venter boasts he will be the first to fully synthesise a life form.

Venter is recognized for pushing the boundaries on the commercial exploitation of life. He has sailed his luxury yacht, *Sorcerer II*, with its fully equipped laboratory on board, around the world collecting anything he felt could be of biological value. His expedition was funded by the US government and a great deal of booty came back with him. The rights of the indigenous people of an area were never considered.

Slide 21 - Venter on board



But there is nothing "cool" about it. Many scientists feel this is gross irresponsibility. For this maverick, the genome – human or otherwise – is simply a commercial commodity.

Venter claimed his expedition discovered almost 4000 new gene families not previously known, and ten million new genes. He described these as "design components of the future." He will, of course, patent most of them.

Ironically, his institute is also one of three heading a study on the ethics of synthetic biology - a clear case of the fox guarding the hen house. The scientific fraternity recognise this as a pre-emptive strike against critics.

Let us look at alien genetics.

Slide 22 - Alien genetics

These scientists build models of life using unnatural genetic systems.

Steven Benner, a biochemist based at the University of Florida, is a pioneer of synthetic biology. He builds models of how life might function using unnatural genetic systems. He said, and I quote to you: "I suspect that, in five years or so, the artificial genetic systems that we develop will be supporting an artificial life-form that can reproduce, evolve, learn and respond to environmental change."

Many scientists shudder to think what form this organism will take. Even if the promoters fail in this attempt, we do have the threat of more effective bio-weapons.

Slide 23 – Bio-weapons

From what I have shown you, you can see that it is possible to construct a dangerous pathogen just using mail-order parts. I will give you a couple of examples that illustrate the concerns of responsible scientists.

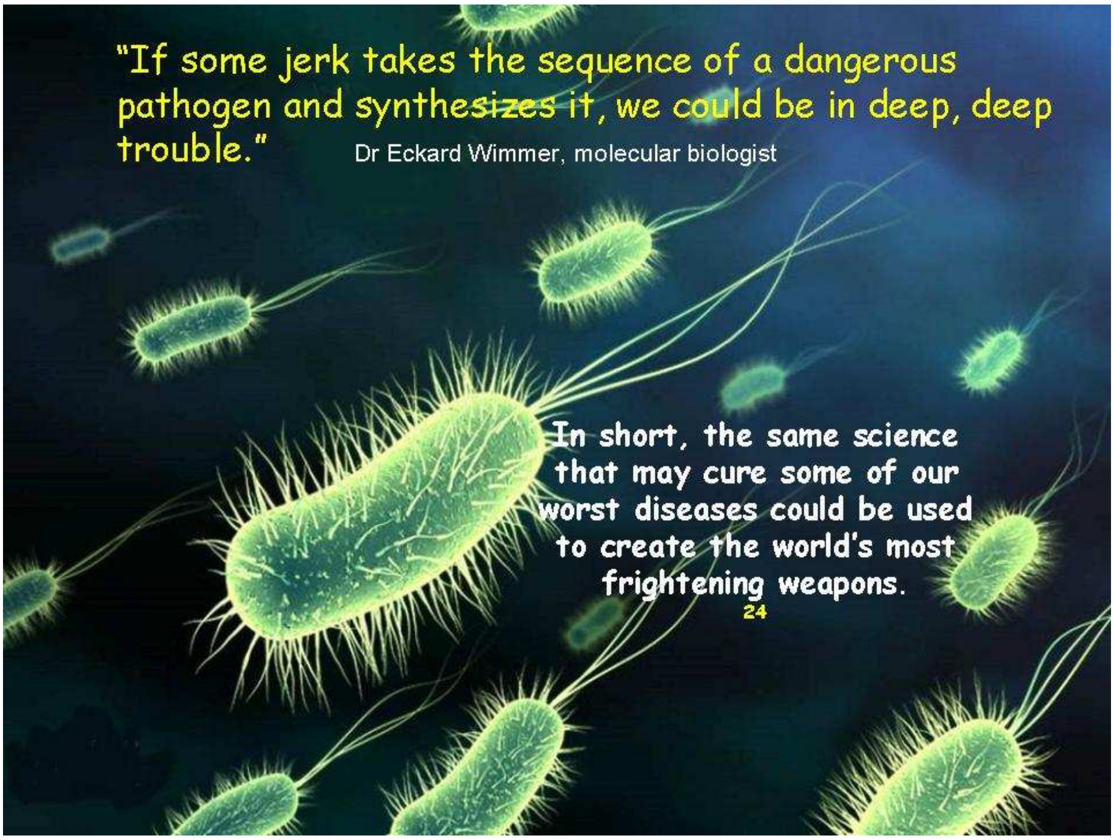
- Dr Eckard Wimmer of New York State University, mail-ordered the necessary components and produced one simply to illustrate that it can be done. Wimmer and his team were immediately attacked as being irresponsible. Of course, the whole point of undertaking the experiment was to illustrate that it was possible to construct dangerous pathogens using mail-order parts. In July 2006, Wimmer told the *Washington Post*, "This was a wake up call." Indeed it was.

- The H1N1 1918 Spanish Flu virus was highly lethal. It has been estimated that it killed up to 50 million people worldwide, conceivably half the then population. Even so, this virus has been reconstructed. Researchers at Mount Sinai School of Medicine in New York and the US Centres for Disease Control were the first to announce that they had resurrected this lethal virus. And guess what? They published details of the completed sequence in the Journal *Nature* for anyone to copy.

As biologist, Jan van Aken, of the Bioweapons Watchdog group, said: "It is unconscionable to recreate this dangerous eradicated strain that could wreak havoc if released, deliberately or accidentally."

Slide 24 - If some jerk...

Dr Wimmer put it succinctly.



Let me further illustrate this madness for you.

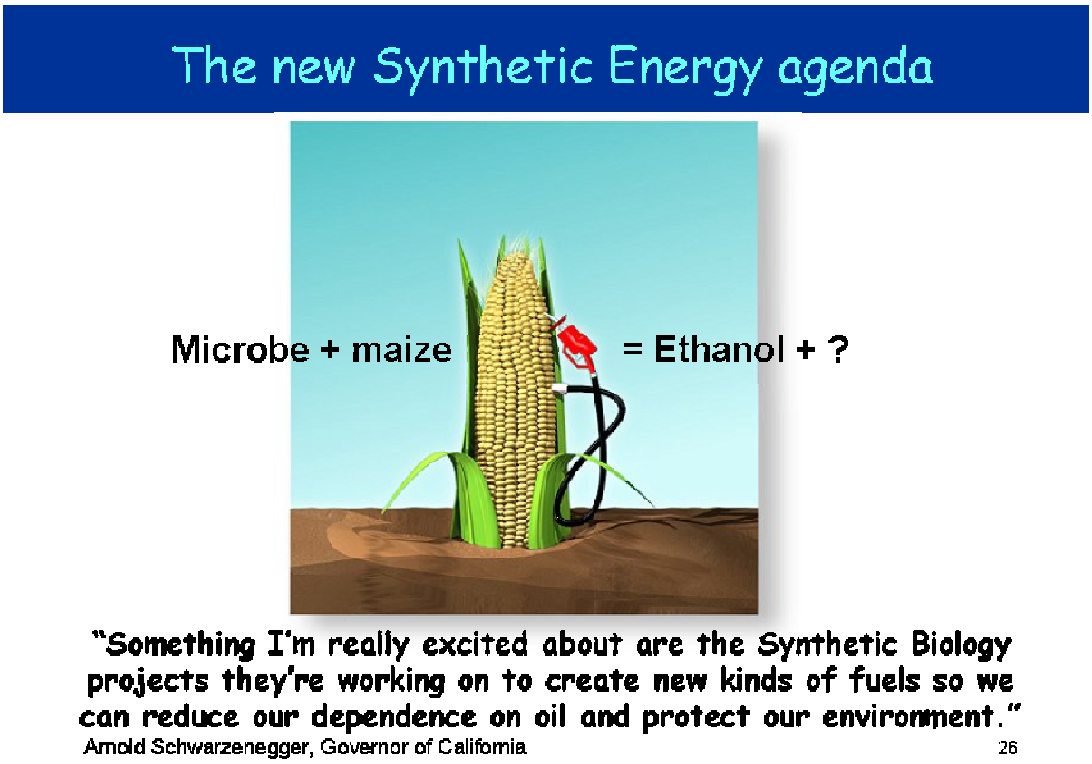
In June 2006, a journalist from the UK *Guardian* tried an experiment. He ordered a fragment of synthetic DNA of Variola major - the smallpox virus - from a commercial gene company. This was duly delivered to his residential address.

It illustrates just how outrageously easy it is to obtain these building blocks of life.

Slide 25 - Biofuels

Leaving the pathogen issue for the moment, let us look at biofuels.

One of the uses proposed for synthetic biology is to produce ingeniously designed microbes to generate biofuels. At first sight, this seems an excellent use for the technology. Synthetic biology's promoters are hoping that this promise of a "green" techno-fix will prove so seductive that the technology will win public acceptance despite its risks.



As you can see, even Arnold Schwarzenegger, Governor of California, has high hopes for this development to help stave off the effects of diminishing oil resources.[1]

In his 2006, State of the Union address, US President, George Bush, announced that his government would devote, "additional research funds for cutting-edge methods of producing biofuels." Synthetic biology is one of the "cutting-edge" methods he was alluding to.

The growing enthusiasm for biofuels in the US stems from recognition that oil supplies in "volatile" parts of the world may not be easily acquired through trade deals or wars. It also deflects attention from tougher tasks like cutting energy consumption and promoting conservation.

There is a rush to plant crops to be used in energy production. In the global south, this has shifted land away from food production. And this trend compromises food sovereignty. Millions of acres of maize grown for ethanol production will divert food crops away from feeding our growing world population.[3] Already large-scale, export-oriented biofuel production in the global south is having disastrous impacts on soil, water, biodiversity, and the livelihoods of peasant farmers and indigenous peoples.

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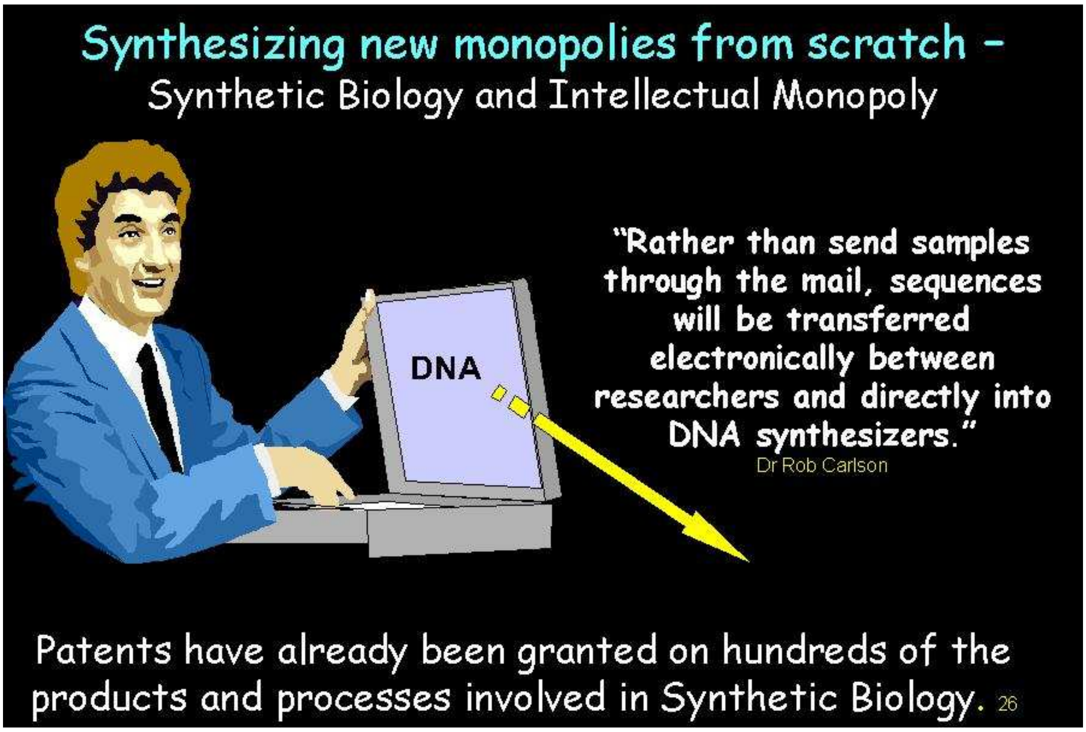
[1] See lecture on "Peak oil: the end of cheap oil – remaking our lives"

[3] See 'Biofuels are driving food prices higher' http://www.theguardian.com/global-development/poverty-matters/2011/jun/01/biofuels-driving-food-prices-higher

Slide 26 - DNA on a laptop

A further question is how will the development of synthetic biology affect intellectual monopoly?



The law states that you cannot patent unaltered genetic material in its natural environment. However, once it is modified, genetic material - including synthetic DNA - becomes fair game for patent claims.

What are the effects of such patents? One is that the fear of patent infringement effectively smothering research that could be beneficial to us all. We saw this happen with the patenting of a gene that causes breast cancer. Many valuable research projects had to be abandoned, lacking for one the research funds to pay royalties or technology fees.

Patenting also enables massive profiteering.

As I have shown, DNA information is now easily transmitted. Genetic data will be the leading edge of information that will change our world. With the ability to electronically transfer genetic information, DNA databases could become as user-friendly as Google.

Biologist, Tom Knight, put it this way: "Pretty soon, we won't have to store DNA in large refrigerators. We'll just write it when we need it."

The cornerstones of today's digital DNA systems are International Databases such as the DNA Databank of Japan or GenBank in the US. Let me give you some idea of the sheer size of these archives.

As of October 2006, GenBank, had digitally stored over 66 billion nucleotide bases from more than 205,000 organisms. Scientists like Craig Venter are working with Google, to generate a gene catalogue to characterise all the genes on our planet.

Now think about this ... every animal … every plant … and every organism … stored digitally.

Slide 27 - Storing diversity

It sounds like something from the Star Trek series and we can make it sound far-fetched, but right now it is very real.

Today's biopirates, such as Venter, collect biological specimens in diversity-rich areas - particularly in the Southern Hemisphere. Instantaneously, they "beam" samples back to far-away laboratories without relying on an overnight courier. The combination of rapid "lab on a chip" gene sequencing and fast DNA synthesisers means that it will be possible to turn DNA samples into information at one location and send them digitally to another. They can be reconstructed as organisms anywhere else on the planet.

This makes bio-piracy very easy indeed.

Slide 28 - Stealing from the natives

What effect will these patents have on indigenous peoples? Let me illustrate just one for you.

Syngenta is the world's largest agrochemical corporation. In 2002, it filed a 323-page patent application relating to its rice genome research. It claimed monopoly control of gene sequences that were vital, not only for rice breeding, but for dozens of other plants as well. The scope of this patent was unprecedented. The claim extended to at least 23 other major food crops.

Civil society violently opposed this and the application was eventually abandoned. But this illustrates the threat of potential claims on digital DNA.

Far-reaching impacts on poorer nations, and the livelihoods of their peoples, are likely to come if synthetic organisms start to displace existing commodities. Here is a simple example.

Synthetic biology's attempts to make rubber would have dire consequences for all native rubber growers[1].

[1] See lecture on "Nanotechnology"

Slide 29 - Trust us, we're experts

Dr Jonathan Tucker put it succinctly:

"The risks attending the accidental release of such organisms from the laboratory would be extremely difficult to assess in advance, including its possible spread into new ecological niches and the evolution of novel and potentially harmful characteristics."

We just do not know the risks involved with synthetic biology or nanotechnology.

For all the talk about synthetic biology's genetic circuits and off-the-shelf parts, a living organism is not a predictable machine. DNA can be transferred to naturally occurring bacteria via the process of 'horizontal gene transfer.' It can then alter the behaviour of natural microbiological systems – affecting the environment in unforeseen and unpredictable ways.

The Asilomar Declaration of 1975 - which covered Potential Biohazards of Recombinant DNA - is often portrayed as a shining example of responsibility by the scientific community, acting for the greater good of humanity. In reality, it was a move by a hand picked group of elite scientists to pre-empt government oversight by promoting an agenda of self-regulation. Sue Mayer of GeneWatch put it this way:

"Scientists creating new life forms cannot be allowed to act as judge and jury. The implications are too serious to be left to well-meaning but self-interested scientists."

Although nano-medicine is being touted as a solution to pressing health needs in the global South, it is being driven from the North. It is designed primarily for wealthy markets. The promise of cheap drugs for the poor may end as it did for many biotechnology promises, a promise still blowing in the wind. Further, questions remain about the health and environmental impacts of nano-materials that are being used to develop nano-medicines.

If current trends continue, synthetic biology and nano-scale technologies will further concentrate economic power in the hands of multinational corporations. Already the food industry is taking advantage of the products of synthetic biology and nanotechnology.

Slide 30 – Nano-foods

As to what nano particles will do when ingested by humans, we have no credible research.[4] The field of "nano-toxicology" is awash with uncertainty. More to the point, little money is being directed to expand safety research. No government anywhere in the world has developed regulations that address basic nano-scale or synthetic biology safety issues.

Because of its unparalleled breadth and scale, nanotechnology has been described metaphorically as a "technological tsunami." A 2005 report from the United Nations' University, 'State of the Future,' warns that, "the accelerated introduction of new technologies – including nanotechnology – is outrunning governments' capacity to understand them." If this is the case, then we have a lesson to learn here.

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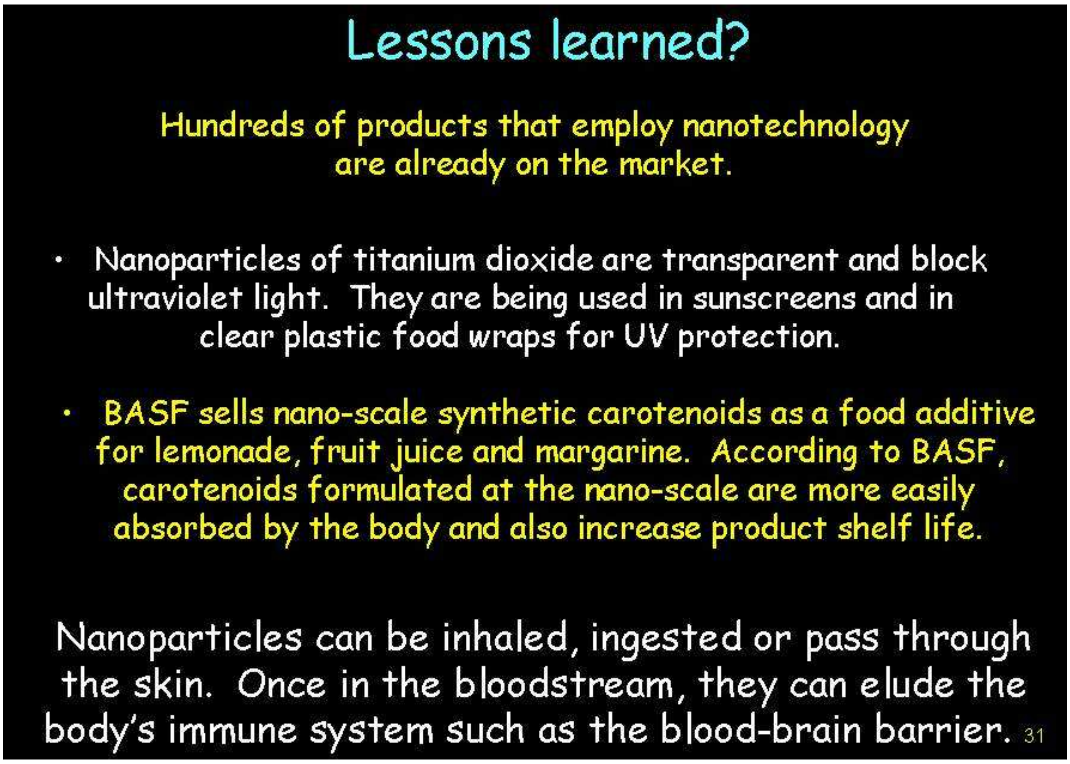
[4] Reports coming from China in 2009 detailed seven women, exposed to nano-particles in an inadequately ventilated workplace, becoming seriously ill. Two subsequently died. Using transmission electron microscopy, nano-particles were observed lodged in the cytoplasm and caryoplasm of pulmonary epithelial and mesothelial cells, and in chest fluid. http://erj.ersjournals.com/content/34/3/559.full

Slide 32 - Lessons



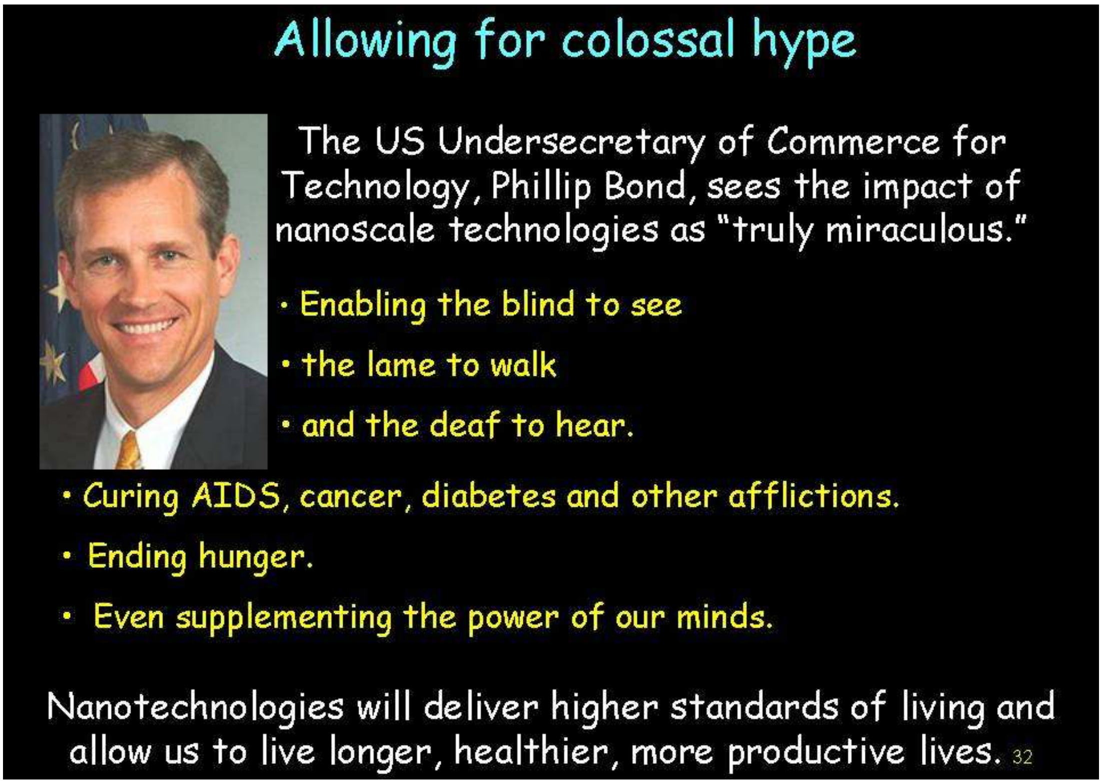
There are many risks to deal with, with any new technology, especially nanotechnology and synthetic biology. And there must be a broad societal debate on these new technologies.

We need to look at the wider socio-economic and ethical implications, including potential impacts on health, the environment, human rights and security. Broad patents on synthetic biology and nanotechnology will be used to consolidate corporate power over the parts and systems of life. How likely is it that the poor will benefit from a technology that is outside their control? It is vital that these building blocks of life are not privatised.

Another aspect of these new technologies is the hype surrounding them. It pours from the media and government ministers who have little real understanding of the science. I will read you this from 'The tiniest science' which appeared in the New Zealand *Listener* on 24 March 2007. Speaking of Don Eigler, described as "a grandee of science" who spoke at a nanotechnology symposium, the article said he is convinced that nanotechnology will permeate almost every aspect of human life. "The impact is likely to grow very dramatically. And much of the impact you'll never know about because it doesn't matter to you if you've got nanoparticles in your sunscreen. It matters to you that your sunscreen works."

Slide 32 - The hype

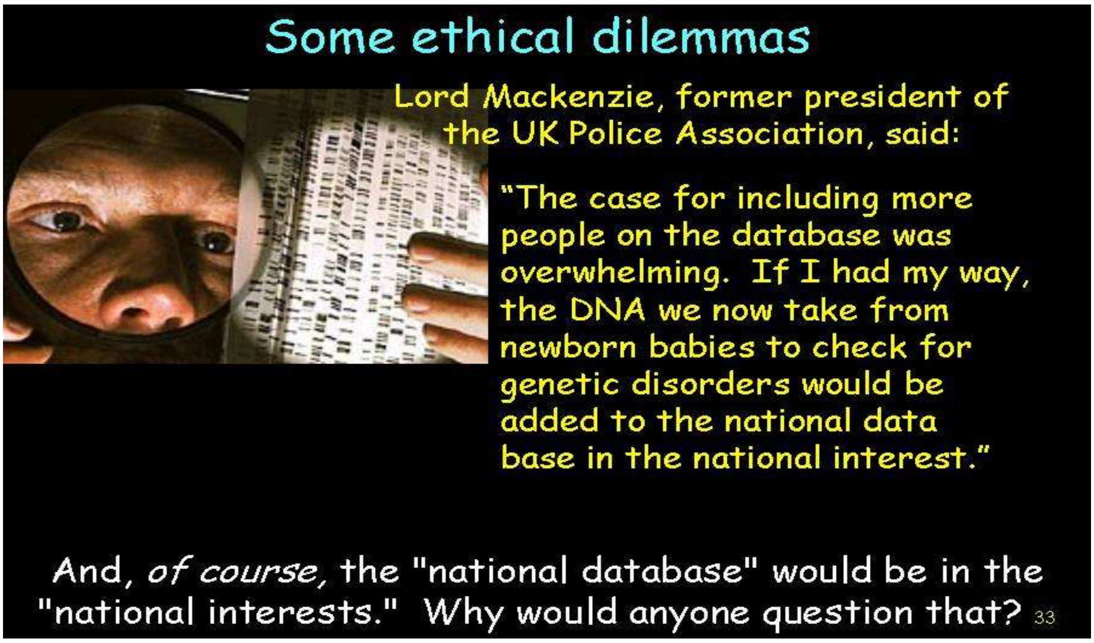
Let me give you another prime example.



This is snake oil salesmanship at its very best. This sort of propaganda needs to be taken with a hefty pinch of salt. The biotech revolution gave us many similar promises - few of which have materialised. In the rush to promote these new technologies, there are serious ethical consequences looming.

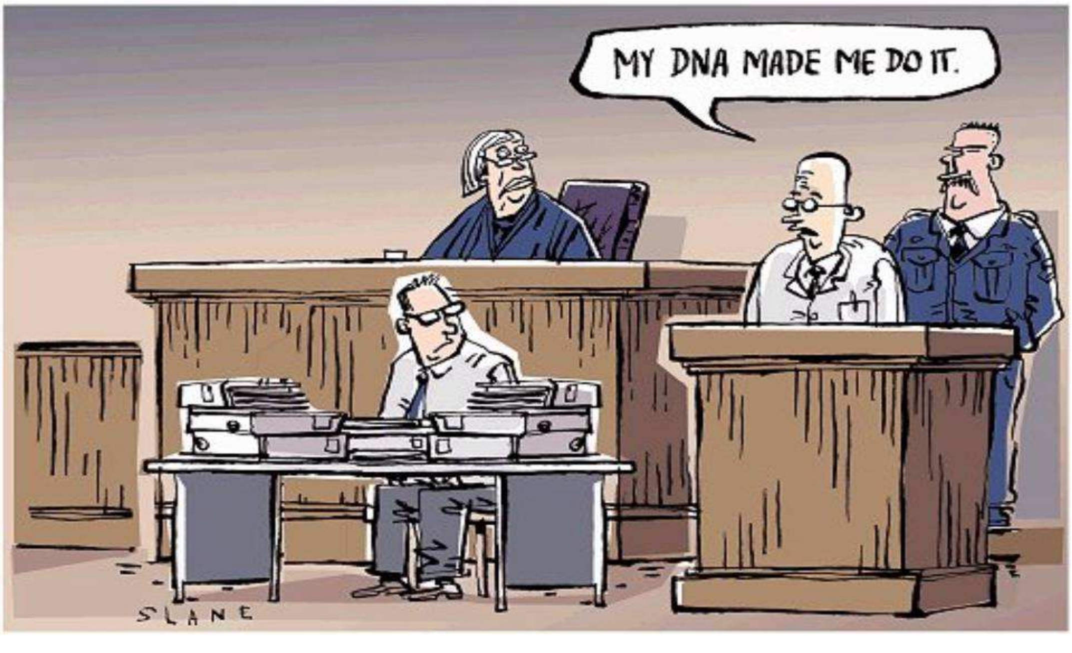
Slide 33 - Ethical dilemma

From this lecture, you will have seen that DNA is a valuable item; one's own even more so.



So who will end up owning your DNA? DNA contains an individual's unique genetic code. It tells a lot about who you are. Will this information be available for just anyone to use? In the US and other countries, the beginnings of genetic profiling are well under way. There are no protocols that protect the information from being leaked. There is no proof that the information cannot be tainted or manipulated once it is in the database. Will there be a law that protects me from my DNA being used against me if it is found on a road or sidewalk? There could be some advantages of course…

Slide 34

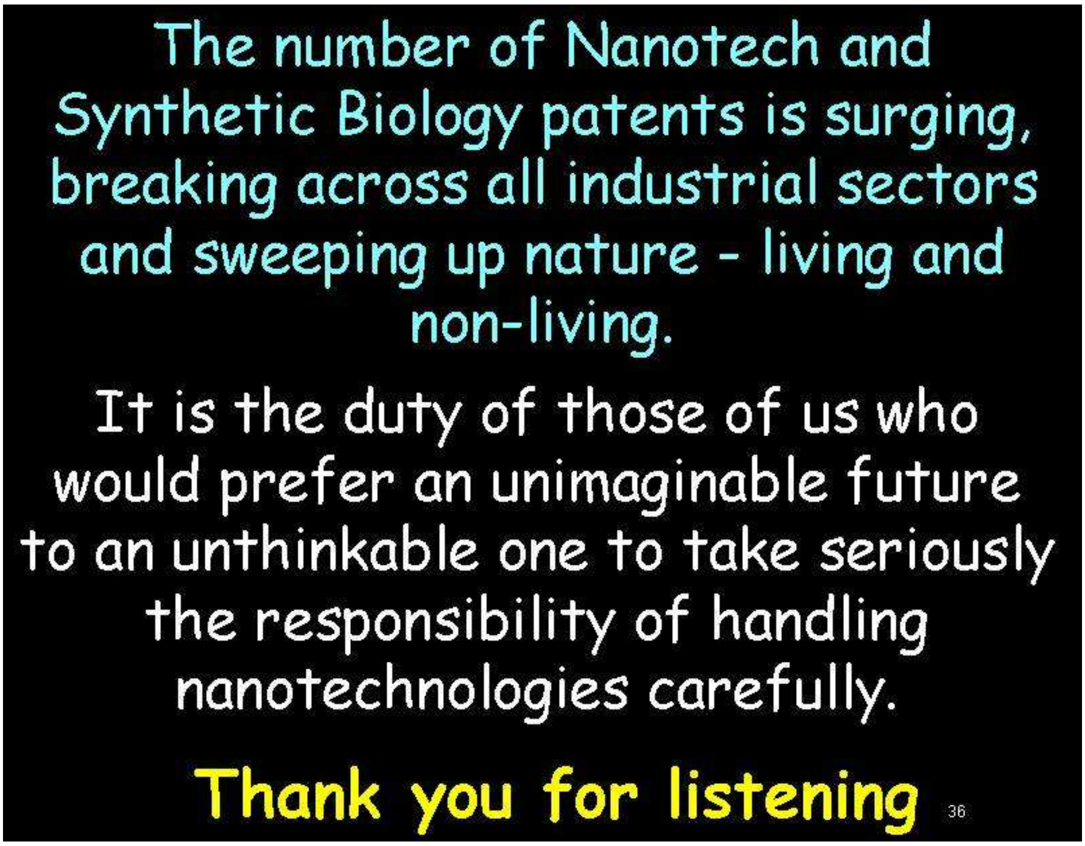


Joking aside, any database could become accessible to big business. Centres could open where one could take a strand of hair and get a print out of someone's genome, get a list of diseases (present or potential), physical defects, life expectancy. Perhaps that is in the future, but we have to remember that what we do now will affect our future generations. As a society, do we want our government to have a record of our genome and have the power to know everything that makes us the person we are? All of these questions need urgent answers.

Slide 35 - Risks

I have shown you just a small peek through the window of these astonishing converging technologies. The ability to construct synthetic organisms from off-the-shelf DNA has the potential to revolutionise our world. As I've also shown, there are serious scientific and ethical issues to consider.

Slide 36



There is material on Craig Venter available on the Internet. Here I will answer one claim he has made.

Dr Venter states that there have been no accidents in biotechnology (genetic engineering). This is incorrect. Here is just one.

Australia suffers scourges of mice, often enough for this to be a major problem. Literally millions of mice congregate and move across a wide area creating a major problem for farmers and the food industry. These scourges triggered scientists to work towards developing a biological contraceptive virus to solve the problem.

While engineering a mouse pox virus, these scientists were shocked to observe that it wiped out all of their laboratory mice, even those that had been vaccinated against mouse pox. In short, the scientists found the extra gene they had inserted had the effect of suppressing the immune system of the mice, which, of course, combats viruses. The result? Laboratory mice normally resistant to the virus also died. Further, it reduced the efficacy of the vaccines used to protect the mice.

As Professor John Richards of the Australian National University, said: “The knowledge gained from this particular discovery alerts us to previously unknown, yet significant, implications."

Lecture ends

Sadly, Robert Anderson died in December 2008.

Following a career in teaching physics, chemistry, mathematics and nuclear medicine at tertiary level, and to meet the public's right to be independently informed, Bob lectured widely on issues of science, the environment and social justice. In the last decade of his life, he authored eleven books and regularly wrote for a number of periodicals. Some of that material can be found on www.connected.gen.nz.

Bob was a Quaker, teacher and writer, a Trustee of Physicians and Scientists for Global Responsibility (www.psgr.org.nz), a member of Amnesty International, a Theosophist, and a campaigner for peace and disarmament. He believed everyone has the right to equality and respect, freedom of speech and religion. He was passionate about making this world a better place for the generations to come.

Enquiries for books written by Robert Anderson should be addressed to connectedbooks@clear.net.nz.