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COMPLEXITY AND CATASTROPHE

A Conversation with Sir John Maddox

[March 1997]

> *My guess is that if the question of human extinction is ever posed clearly, people will say that it's all very well to say we've been a part of nature up to now, but at that turning point in the human race's history, it is surely essential that we do something about it; that we fix the genome, to get rid of the disease that's causing the instability, if necessary we clone people known to be free from the risk, because that's the only way in which we can keep the human race alive. A still, small voice may at that stage ask, "But what right does the human race have to claim precedence for itself?" To which my guess the full-throated answer would be, "Sorry, the human race has taken a decision, and that decision is to survive. And, if you like, the hell with the rest of the ecosystem."*

Sir John Maddox and John Brockman at the *Edge* London Science Dinner January 24, 2006

Introduction

Sir John Maddox, editor of *Nature* for 22 years (1966–73 and 1980–95), was the dominant figure in a golden age of science. A fierce proponent of reason, rationalism, and science-based thinking, he built *Nature* into the premier publication of its kind, while still retaining the respect of the international science community for his intellect and writing. His friendship meant a great deal to me, as did his support and encouragement of *Edge* and the third culture.

In this discussion he talks about what we need to be concerned about: the increasing accumulation of data on a huge scale, lack of quantitative progress in biology, infection, impact, cloning, and the stability of the human genome.

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SIR JOHN MADDOX (1925–2009), who served 22 years as the editor of *Nature*, was a trained physicist, who has served on a number of Royal Commissions on environmental pollution and genetic manipulation. His books include *Revolution in Biology*, *The Doomsday Syndrome, Beyond the Energy Crisis*, and *What Remains to be Discovered: The Agenda for Science in the Next Century.*

COMPLEXITY AND CATASTROPHE

MADDOX: There's an extremely interesting question that seems to me to be very urgent: How on earth is science going to cope with the accumulation of data, on a huge scale, of recent years? This relates to another question that hasn't been given enough attention in recent years: When on earth is biology going to become a quantitative science, like physics and chemistry—when there's good evidence to believe that it can't make progress in some fields without becoming much more quantitative?

The most successful efforts have come from the study of fear. Fear is a relatively tractable emotion, unlike love or hope which are difficult to pin down. It's always easier to study brain functions that involve clearly defined stimuli and responses than those that don't. For fear, you can easily create experimental situations where the onset of a simple stimulus that warns of impending danger elicits a set of stereotyped responses in an animal, like a rat, that are very similar to the kinds of responses that occur in a human facing danger. By following the flow of the stimulus through the brain from the stimulus processing pathways to the response control networks, it's possible to identify the basic neural circuits involved. We've done this for fear.

Let me give an illustration of what I mean. In a field like cell biology, everyone now has a clear picture of how the cell cycle is driven. You have proteins called cyclins, which are meant to interact with another protein called Cdk. Cdk plus cyclin activates two successive steps essential to the cell cycle. One of them is the replication of the cell's DNA; the other is the actual fission of the cell into two daughter cells. It seems to me high time that people recognize that the complexity of this system is so great that it can't really be dealt with in the simple way in which textbooks ordinarily deal with description, i.e., the explanation of events.

If, for example, you have an ordinary bacterial cell going through the process of cell division, it may be prompted to do that by some external signal in the environment; it may be prompted to do it simply because time has passed—twenty minutes is the length of time it takes the E. Coli to divide into two, and maybe just twenty minutes is up. There are several different molecular influences acting on this complex of cyclin and Cdk which is what actually triggers off the cell division. The complexity of the problem is so great that you can't comprehend it in the language I've been using; you can't comprehend it in the language of the textbooks, because it has become a mathematical problem. Nevertheless, very few people take this seriously.

There's more to it than that. I'm advocating that in the case of the cell cycle this is a specific biological problem. How do we understand the cell cycle? What makes a cell divide? What can we say about the competing influences on a cell—the external environment, the internal need of the cell, the need of some other cell in the same organism? How do these competing influences conspire to decide that the cell is now going to divide into two? What we need are mathematical models for saying what actually goes on.

There are other fields like that. Take the way in which the muscles in our arms work. Any molecular biologist will now tell you this understanding is one of the big triumphs of the past ten or fifteen years, that muscle fibers are made of actin and myosin, two proteins—and the idea is that the myosin molecule, which is smaller than the actin molecule, acts as a kind of enzyme at the head of the actin fiber, that can ratchet itself along a parallel actin fiber.

Molecular biologists say, ah, we now understand how muscles contract. But nobody has done the thermodynamics of this problem. It's obviously a matter of great interest to the world at large to know how much energy is used. The molecular biologist will tell you it comes from ATP. ATP, adenosine triphosphate, is actually the universal source of energy in living cells, and everyone says that's fine, but actually what are the thermodynamic aspects? This question is not considered, and it's a crucial question, because that's the kind of consideration that would tell us when it is that muscles become tired, when they no longer function, or when they become rigid, and go into spasm. There are all kinds of important abnormalities in muscle behavior that would be explained by thermodynamics, if people put their minds to the task. The molecular biologists may have answered the "how" question, but they will not be able to answer the "why" question until somebody has done the thermodynamics.

What I'm saying underneath all this is that perhaps molecular biology got itself into the condition in which it's far too easy to get data, and therefore there is no incentive to sit down and think about the data and what they mean. But I'm sure that as the years go by, and not many years, people are going to have to be thinking much harder about how they get accurate quantitative data about the behavior of cells, muscles—all these things in living creatures.

JB: What is the relation of the acquisition of such data to the development of technological tools that allow you to formulate models and execute on those models. Are your perceptions related to the development in increased computational power?

MADDOX: The case I'm making actually doesn't depend on the improvement of computer technology, but what you say is absolutely right; that to solve some of these problems is going to require unprecedented computer technology. But let me illustrate it this way: suppose you want to understand how a cloud functions, a cloud in the sky. Sometimes you get rain out of a cloud, but not always—you see clouds up there but no rain coming out of them. Why is that? The reason is that in a cloud you have a constant upward and downward flow of drops of water, particles of ice and so on, and it's in a dynamic situation. For every cloud the bottom is at some temperature and the top is at another temperature—a lower temperature, of course. Sometimes this dynamic stability of the cloud becomes unstable, perhaps because there's a shift of the temperature, perhaps because something goes through it like a projectile, an aircraft perhaps which may leave a trail of condensation behind it if it's travelling through the humid atmosphere, But you can only understand cloud behavior and answer the question when will this cloud produce rain, if you have a model which can be in that case quite a simple model.

In the case of the cell and the cell cycle, it's a much more complicated model I'm looking for, and there in reality one would need supercomputers to handle the model. The models people have built so far—I'm thinking of John Tyson at the Virginia Polytechnic and Albert Goldbeter at the Free University in Brussels—have been handled on ordinary desktops, but everyone agrees they're not sufficiently refined. Once you start refining them you get into real problems. But there's some parts of science that can only be understood when you make a model. The cell cycle is one, the muscle is another, and each of them, being biological problems, are very complicated.

JB: Speaking of cells, let's jump off this track for a minute and talk about the cloning experiment in Scotland. People are having a hard time getting their heads around it.

MADDOX: I look at the scientific importance of that experiment in the following way: it seems to me is that it is a demonstration that you can take an ordinary cell from a person's body, a somatic cell as it's called, and recreate the genome from that. The reason that's interesting and important is that up until now people haven't been sure whether the DNA in every cell of our body retains the power of making an embryo. This experiment shows that that happens. You can in principle take a cell from your skin or anywhere and make it into an embryo which then grows up into a person. That rules out a number of possibilities for the ways in which different tissues of our body have their different characteristics. Now a liver cell and a kidney cell are outwardly very different; a skin cell and a nerve cell are very different to look at, in their properties, and their behavior. But in practice, the difference could be because their genes have been changed in some way. This experiment in Scotland shows their genes have not been changed radically. They've been silenced, perhaps, but only temporarily. That's very important.

Now as to the practical importance, it seems to me that the immediate value of it is in animal husbandry, and that is in those fields where people have been trying to use sheep, or pigs, or cows, to generate biochemicals—to make medicines in sheep. There's a lot of interest in this. The procedure is quite simple: you introduce the human gene responsible shall we say for making insulin, into sheep, and then you collect the insulin from the sheep, and you find it's human insulin, not sheep insulin. Thus you have natural human medicine generated on a farm.

This kind of work is very difficult, because it's very much a matter of chance to where the human insulin gene will go. If you can take a successful chance, a case where the gene has gone in the right place and it's producing in the sheep a lot of insulin, then you can clone that sheep and get many, many other sheep. You don't have to rely on chance any more. So that's going to be the immediate practical value.

The dangerous question is what happens when people start doing it to themselves—to people. For what it's worth, in Britain and many other countries, it's against the law to do this; it's a criminal offense to manipulate the human embryo beyond 14 days of life, and it's in fact a criminal offense to do so without the approval of a licensing authority. How effective that interdiction would be in other countries is anybody's guess. My guess is that countries like Morocco, which has been in the vanguard of sex change operations for many, many years will be in the vanguard of people cloning. So in that spirit, it's a question of waiting to see how the technology works out, and trying to get some kind of international understanding on the circumstances where it would make a lot of sense.

Are there any circumstances in which it would make a lot of sense? I can think of one. Coming back to one of the other questions I mentioned at the beginning, suppose we got into a situation where we had reason to believe that there was something wrong, something inherently wrong, with a set of genes that people have inherited, which have been evolved, of course, over the past four and a half million years, since we separated from the great apes. Suppose that we had reason to believe that one of those genes was going to cause trouble as time went on. For example, there is a case which one shouldn't make too much of, but's it's an illustrative case, of Huntington's disease, where there's a normal gene in every one of us, which makes a protein called Huntington—nobody knows what its function is. This gene—this gene at cell division, when people procreate, produces a bit of nonsense at the end, and if the bit of nonsense is longer than a certain amount, it actually gives a person Huntington's disease—and he or she dies. That's bad news. There are half a dozen other diseases like that, same unbalanced mechanism. If there were a lot of those incidences, you could pretty well say that the time will come in the evolution of people when we'll all be dying of Huntington's. One way of avoiding it would be to clone people who didn't have this propensity. That's about the only circumstance in which I can see people cloning, as the last resort for the human race to avoid a calamity that would be brought about by gross instability of the human genome. I'm not saying that this is a real prospect now, but maybe in a hundred generations it could be.

JB: What other areas are causes of concern to you?

MADDOX: I've got a very simple view about the environmental problem that we all know about which is that a great deal of the excitement there's been in the past 25 years about the environment can be boiled down to this: one can say look, you can get whatever environment you wish, provided you are prepared to pay for it. You can get air as clean as you like, water as clean as you like provided that taxes, and the regulation of the private sector is tight enough to meet the standards laid down. This does mean, of course, that the countries that can afford a clean environment are the rich countries, and the environment they purchase is a big purchase—sometimes out of public funds, sometimes out of private funds. Poor countries can't afford a decent environment, but as they get rich they will enjoy the wealth necessary to make them see that a clean environment is good for them.

The real environment problems now, it seems to me, are things like infection. We've had AIDS pop up since the early 1980s; it's been a big shock to people that there could be such a completely novel disease doing such terrible damage and apparently untreatable by existing remedies. It's my belief that there must be many other diseases like this waiting for us as the centuries tick by. Suppose, for example, that there were a really infectious cancer virus, something which could just give you lung cancer if you took it in as if it were flu. There's only one known human cancer virus at present, but there are many in the cases of domestic animals like cats, such as the leukemia virus that's well known. The only human cancer known is papilloma virus which causes cervical cancer. And we all know that quite apart from these bizarre novel viruses, there are ordinary bacteria, like E. Coli, that from time to time acquire mutations that make them more virulent. The new E. Coli strain 170, for example, has caused a lot of damage in the United States, in Japan, and now in Britain. Dozens of people have died of food poisoning, in effect.

These bacteria are going to become more and more common as the years go by because we are putting the bacteria under such enormous pressure with the intelligent use of antibiotics in hospitals, curing the sick, and so on, the bacteria really have nowhere to go unless they become more virulent.

So we must expect that however good the defenses are—by defenses I mean the drugs, the hygiene—the bacteria are going to keep on getting more virulent unless they can be really hit hard. We have the prospect ahead of us of increasing threats from viruses and bacteria, and the organisms that cause diseases like malaria. It's actually part of the price we pay for living longer, for being healthier. It's just one of those things, something that one ought to reckon with, not wring one's hands about.

There's another worry, one which perhaps sounds unreasonable. I believe that it's only a matter of time before the world will have to plan to avoid catastrophe by the impact of asteroids. It's now known that 64 million years ago the Cretaceous Period and the dinosaurs were brought to an end because there was a big impact of an asteroid ten kilometers across—about six miles across—the impact site has been found on the Caribbean coast of Mexico, and the crater it left in the ground is 180 kilometers—about 110 miles across. It put up dust into the atmosphere, and the dust stayed there for so long that the vegetation died off, and the dinosaurs that ate grass died off with it, and lots of other species as well. That kind of event is likely to recur every few tens of millions of years.

Luckily, the techniques are good enough to be able to pick up about 90 percent of the objects that size in the neighborhood of the earth. They're called asteroids, or they may be comets. The biggest difficulty is that of a cometary impact because comets travel at a faster speed than asteroids and the warning would be less. But if you think that the whole world was put to an end 64 million years ago pretty well, by one impact, is it not sensible that the human race should do something to protect its own stake in the future? I believe we should be planning to do something about events like that that might happen in the future. Of course smaller impacts can do a lot of damage too. I think it's only a matter of time before people will be setting out to track those things, and to destroy them.

JB: How will this be implemented?

MADDOX: There are lots of very interesting problems that people haven't really thought about; for example, the best way of avoiding an impact is to explode a nuclear weapon near the projectile. If you can catch it early enough, shall we say several days before it's going to hit the earth, then a quite small nuclear weapon, shall we say 100 megatons, would be enough to nudge it in one direction or the other, but the most efficient way is actually to slow it down; to explode the thing in front of the asteroid. There are a number of associated hazards—if the explosion were not absolutely accurately timed, it might blow the asteroid up, and that might seem good news except there would then be several fragments, and one of those would certainly hit the earth, and it might still be quite big. So the best thing is a carefully controlled explosion to nudge the thing away.

The trouble with that is that the Russians and the United States are now against the deployment of nuclear weapons in space; the Chinese are probably against the development of other people's nuclear weapons in space; nobody has talked about the question anyway. So the idea that it might be announced there's going to be an impact a year from now wouldn't actually leave enough time for people to get around the table and decide what best to do about it. My own opinion is that there's going to have to be rather formal negotiation quite soon on what would happen if there were an impending impact. There would have to be arrangements that would make sure that no nuclear weapon authorized for use under this program could be used to divert an asteroid onto some sensitive part of the world, like China or Russia—and so on. All kinds of problems.

JB: How much time would we have?

MADDOX: It depends. In the worst case there would be hardly any warning at all—a couple of days. A couple of days is too little time to do anything. And the chance that a large object, ten-kilometer object, would arrive with only two or three days' warning is probably about ten percent. No program that one can think of devising is going to avoid the worst case—you can't get absolute security—but you could at least hope to get rid of ninety percent of the big impacts.

In the case of asteroids, the warning probably would be quite long, possibly even two or three years, because these asteroids make circuits about the sun just like the planets do, but they go in eccentric orbits, which is why they can hit the earth. This means that if you pick one up on a particular orbit, you might be able to figure out that on its next orbit, or its next but one, it's going to hit the earth. You've got quite some time to plan what to do in that case. And the feasibility of doing something will of course improve as time passes, so in that case one could begin by hoping to avoid half the large objects, quite soon, and, maybe in a hundred years, to avoid ninety percent of the large objects. However, we'll still be stuck with the problem of the ten percent.

JB: How do these ten percent sneak in?

MADDOX: They begin as comets and the thing about comets is that nobody is entirely clear how they find their way into the inner solar system. The theory—and there's no confirmation of this at all—is that right at the edge of the solar system, roughly at the place where the sun's gravitation field is comparable with the gravitational field due to external objects, like molecular clouds, other stars, and so on—there's a cloud of cometary material called the Oort Cloud, named after the Dutch astronomer Van Oort. What's said to happen is that these objects are either deflected into the solar system by a passing star, or attracted in by some conjunction of one of the outer planets with Jupiter, so that they start drifting into the solar system.

They spend some time with Neptune, and some time with Saturn, some time with Jupiter, and either they become asteroids, in which case there's relatively little problems, or in some extreme cases they start heading in from the outer region of the solar system, and they just make one pass at the sun. That's the most dangerous case, because these hyperbolic comets, as they are called, are traveling very fast, and they haven't been seen before, and they will only make one pass at the sun anyway. In that case it would really be quite hard to be sure that one could spot them many days in advance of an impact. That would be curtains.

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JB: Ok, we've talked about data handling, infection, cloning, and impact. Going beyond cloning, let's talk about the stability of the human genome.

MADDOX: I dealt with that in the case of the sheep but let me add this to it, because I think it's important. Up until now it's been the assumption of most generations living on the surface of the earth, that the ideal condition of human beings is that in which we recognize that we're a part of the natural world, and our goal is harmony with the natural world. If you think of it, what natural selection, Darwinian natural selection, does, is precisely to make the successful species, those that survive, fit for the environment at the time. It's a device for making sure that everything is in harmony with the natural world. We have accepted, I think, as the human race, that this is indeed the case, that we must accept our dependence on the natural world and our need to be in harmony with it.

What happens, then, if we learn that we are one of those many species destined to become extinct because for some reason or another our genome hasn't worked out to be quite as stable as it might have been. In those circumstances we would have a nasty choice. We would have to decide, would we not, whether or not we let ourselves become extinct, as part of our dependence on nature, part of our being a part of nature, or whether we actually struggle against it; do something about it.

My guess is that if the question of human extinction is ever posed clearly, people will say that it's all very well to say we've been a part of nature up to now, but at this turning point in the human race's history, it is surely essential that we do something about it; that we fix the genome, to get rid of the disease that's causing the instability, if necessary we clone people known to be free from the risk, because that's the only way in which we can keep the human race alive. A still, small voice may at that stage ask, but what right does the human race have to claim precedence for itself. To which my guess is the full-throated answer would be, sorry, the human race has taken a decision, and that decision is to survive. And, if you like, the hell with the rest of the ecosystem.

JB: What are the scientific issues bothering people today that don't worry you?

MADDOX: It's interesting that more than a quarter of a century has passed since the publication of "The Limits to Growth," the Club of Rome document, which seemed to me to produce a far too simpleminded view of the global problem. The global problem is not the shortage of resources. It's true that we are using up petroleum at quite a rapid rate, two billion tons a year, and the amount of petroleum in the surface of the earth is not by any means infinite. But there's a natural balancing mechanism in those simple scenarios of shortage. The balancing mechanism is price. What we're pretty sure of is that we've now used up one dollar a barrel oil; it's all gone. There's some two dollar a barrel oil left in Saudi Arabia, but the Saudi Arabians are very careful about the degree to which they let their stuff be exploited, and that appears on the market at fifteen dollars a barrel like everybody else's oil. So price is really a regulator of scarcity.

Even when petroleum becomes so expensive that it's used only for the production of chemicals—some of the few chemicals that can be produced exclusively from petroleum—the world will not stop. There are plenty of other ways of generating energy which at present are more expensive than petroleum—like nuclear power, even solar power, in small quantities, like hydrogen, which can be made by electrolyzing water, and used as a fuel—so there are all kinds of ways. The future is going to be dependent upon on other sources of energy than the ones we at present use.

The argument that we're using scarce, irreplaceable sources of energy is an argument not worth its salt; not worth listening to seriously. We're using up cheap resources, and in due course we're going to have to use more expensive ones, which is an argument of course for wealth creation, economic growth. So my view of the Club of Rome's argument on the Limits of Growth is just that. It's an economic question, always has been, and it will be in the future and it will be dealt with in economic terms.

But the other environmental problems that seem to me to be much more important, are those concerning the safety of people's lives. After all, the avoidance of pollution is primarily a problem of how do you keep people healthy. That's what the end purpose is supposed to be, keeping people alive and healthy. The big threat there has been, and remains, infection, which we've talked about. It seems to me another is global warming. Global warming is the scenario that's supposed to happen when, because of the accumulation of carbon dioxide in the atmosphere, the temperature on the surface of the earth is increasing. I'm in a very odd position on this. I accept that global warming, because of carbon dioxide, is going to be a reality at some stage in the future. I disagree with the way in which the forecasts have been made by the organization called the Intergovernmental Panel on Climate Change, which is under the UN umbrella, although it's really a child of the United Nations Environmental Agency and the World Meteorological Organization.

These people have produced so far two assessments of the seriousness of global warming, and they predict that during the next century the temperature will increase by between two and three degrees centigrade—which doesn't sound much but actually would be a lot. This is the average temperature, and that would mean that in places like the southern Sahara it would become even more like a desert, and it might even mean that in some parts of the United States, like Texas, it would become a bit like the Sahara.

But the real problem is that all this is based on computer modeling, and while I'm fully enthusiastic about computer modeling as a way of understanding scientific problems, and comprehending large amounts of data, I think it's dangerous to rely on computer modeling when you are trying to make predictions about the real world. In fact the satellites that have been used to measure the temperature show that the temperature is increasing less rapidly than the computer models predict, by a factor of three. So I think that the scenario is less gloomy than the Intergovernmental Panel on Climate Change says.

On the other hand, it's going to happen sometime, and we have to do something about it. It raises the whole question about how do you get an equitable relationship between the rich and the poor countries. The rich countries have to acknowledge that they can't unilaterally deny developing countries the right to follow in the same kind of path as they themselves have followed in their own economic development. On the other hand, the poor countries have to accept that they can't let their demands on the global system increase as rapidly as their populations increase. They have to accept some kind of restraint on population as a tradeoff. That's going to be such a terribly difficult negotiation and it's very hard to see how it could be completed in the next century.

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