Mae-Wan Ho

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Mae-Wan Ho: A brief scientific biography

Peter Saunders

As I'm sure you all know, Mae-Wan spent the last 25 or so years of her life doing both pure science and science devoted to helping our planet and the people who live on it. For the latter she founded the Institute of Science in Society, and edited the magazine *Science in Society*, for which she wrote literally hundreds of articles.

What I'm going to talk about now is not directly related to ISIS – there'll be more about that side of her interests tomorrow – but I still want to take this opportunity to thank everyone who helped ISIS and made its work possible. The list is very long and includes many of you who are here today – and others who are not. It would be impossible to thank everyone but I'd like to mention especially those who at some point were members of the ISIS team: In alphabetical order, let me thank Sam Burcher, Brett Cherry, Emma Haffegee, Jules Haffegee, Lim Li Ching, Angela Ryan, Eva Sirinathsinghji, and Andy Watton. Also people like Eva Novotny who were never formally part of the team but worked with and supported us all the same. And Joe Cummins, who himself passed away some time ago.

I also want to thank the two organisations that were our main source of funding: the Third World Network, based in Malaysia and the Fondation Salvia, based in Geneva. Both supported ISIS for many years, each burdening us with as little red tape as they could manage, bearing in mind that they had to assure themselves and their boards that their money was being spent properly and consistent with their own missions.

But it was more than just not interfering too much. Mae-Wan and I always knew that Martin Khor and Chee Yoke Ling of TWN and Jackie Casimir-Lambert of Salvia were friends, that they had the same aims that we did, that we could discuss issues frankly with them and draw on their experience. It has been an uplifting experience working with you, Yoke Ling and Jackie, and now that ISIS is no more, I wish you the greatest success as you carry on your own work.

I said I was going to talk about epigenetics, and I will, but I'm going to start by saying a bit about Mae-Wan's scientific career. Most of you knew her because you shared an interest, more likely a passion, with her. What you may not have realised is how many other interests she had and how much she contributed to other fields. Most of us would have been happy enough to make as original and important contribution as she did to any one field. She did this in many, as you can tell just by looking at the titles of the talks you'll be hearing over the next two days.

I need to say something about this because her opponents have always tried to dismiss her as anti-science. Nothing could have been further from the truth. Mae-Wan was never against science. She was against bad science, careless science, corrupt science. But she was passionate about good science, far more so than many who call themselves scientists. She demanded very high standards, and she kept to them herself. Many scientists did not like what she wrote, but very few dared to challenge it.

If you ever hear anyone try to cast doubt on her qualifications as a scientist, just remember that she did far more first rate conventional science than most. She published 106 articles in peer-reviewed journals and 62 in collected volumes. That's a lot more than most scientists, and remember, she was never the head of a large group. You can get a long list of publications if your name goes on everything from your lab, but if Mae-Wan was listed as an author she had been closely involved in the research and more often than not had actually written the paper herself. She also worked in many different fields, and this inevitably makes it harder both to produce lots of papers and also to get them published.

Mae-Wan also published a number of scientific books, the best known being *The Rainbow and the Worm* (1993,) and its sequel *Living Rainbow H_2O* (2012). Copies of her last book*, Meaning of Life and the Universe,* published posthumously, are on display at the back of the room. The title, by the way, is typically Mae-Wan. On the one hand, it is a bit of irony: the name comes from the *Hitchhiker's Guide to the Galaxy*: the Meaning of Life, the Universe and Everything. Mae-Wan certainly didn't mean to imply she'd found the answer to that – or for those of you who remember the story, that she could tell us the significance of the number 42. But it was an aspiration, the endless quest that science should be about. Her favourite character in fiction was Don Quixote.

Mae-Wan also wrote 754 of what she called "Popular major works," most of them published in *Science and Society*. She didn't count these in her CV as scientific publications but in fact they were. Articles in *SiS*, as we called it, had to be fully referenced just as if they were in a scientific journal, and they had to be right. If you are going to tell people something that is different from what they will get from conventional scientists and popular articles, then you should tell them exactly why you are saying it and provide the evidence. If some other scientists disagree then they can see the basis for your claim and they are welcome to refute it if they can. And if they cannot, then the lay reader can have even more confidence in what you say.

Mae-Wan used to say that her scientific career began when she was a pupil in a convent school in Hong Kong. She had been taught about the Trinity, but she couldn't make sense of the idea. She spent some time thinking about it and one night she thought she'd got it. The next morning she rushed up to the nun who was her teacher and announced proudly that now she understood the Trinity.

Much to her dismay, the nun neither congratulated her for working it out nor even praised her for taking the religion seriously enough to try. Instead she chastised her because as a Catholic (which in fact Mae-Wan was not) she wasn't even supposed to try to understand the Trinity. She was meant to take it on faith without even knowing precisely what it was she was being expected to believe.

Mae-Wan was to find much the same attitude among scientists. And she always struggled against it, and she kept getting into trouble with the scientific establishment just as she had with the nun – though with the difference that she always spoke of the nuns at her school with genuine affection.

Right from the beginning of her career, Mae-Wan wanted to find the answer to Erwin Schrödinger's famous question "What is life?" That was why she chose to work in biochemistry and become a molecular geneticist. She was successful enough to win fellowships that took her from Hong Kong to the US and then to London; if you look at the first couple of dozen articles in her CV you see she was publishing in high impact journals like *Nature* and *PNAS*. The more she learned about biochemistry and biochemists, however, the less she believed this was where she was going to find what she was looking for, so she gradually moved away from the subject. Later on, however, her years spent in the lab doing molecular genetics turned out to be well spent when she became involved in the debates about genetic engineering.

From that point on, it's harder to follow her career because she was usually working on several different things at the same time. The next two slides list a few of the many papers Mae-Wan wrote. These illustrate the range she was covering: molecular genetics, evolution theory, developmental biology, physics.

I want to fasten on her interest in one particular area, evolution theory. It was her first step outside molecular genetics, and it influenced everything she did after that.

The crucial paper, published in 1979, was entitled Beyond neo-Darwinism: The epigenetic approach to evolution. The argument was in essence like that of D'Arcy Thompson in his famous book of 1917: *On Growth and Form.* What, he asked, is the origin of form? Is it just genes or do physics and chemistry play significant roles? And just as we can ask about form, so we can ask about change of form, i.e. evolution. Is that to be understood simply in terms of natural selection acting on genes, or do we have to look at physics and chemistry and especially the process of development?

The next slide, taken from On Growth and Form, illustrates the point. If we want to understand how those medusoids came to have the complicated shapes they do, should we concentrate on genetics? A lot of biologists would say we should, but they'd have a problem with the one on the bottom right because it isn't a medusoid at all. It's a drop of fusel oil that's been allowed to fall into paraffin. It got its shape from the undirected physical forces that acted on it. Given that, it is surely hard to claim that the best way to study the real medusoids is to fix on genetics and ignore physics.

It was in this context that in about 1940 CH Waddington coined the word *epigenetics.* He defined it to mean everything that happens between the genotype and the phenotype. Development, in other words, though including various processes that we now know occur in the genome and that hadn't yet been discovered.

Waddington took the word from the earlier term *epigenesis*, the word Aristotle used to express his theory that form appears gradually during development. That view was accepted for a long time, with some modifications to suit the Church, but ran into problems when the success of Newtonian physics led scientists to demand explanations in terms of matter in motion.

Modern mathematics and physics have taught us that undirected matter in motion can indeed produce form, as for instance in the drop in the picture, but at the time this didn't appear possible. There seemed to be two quite different ways in which form might be produced. One was through vitalism, the theory that there is some sort of force outside physics and chemistry that directs what happens in organisms. The alternative was preformation, *i.e.* the form was there from the beginning.

You're probably familiar with the homunculus that was supposed to be contained in either the sperm or the egg and simply increased in size during development. Actually that theory didn't last very long, but the idea that form is in some way determined at the start of development persisted. It's still the dominant idea today; the genes are often described as constituting a blueprint for the organism.

So when Mae-Wan and I wrote of an epigenetic approach to evolution, we were arguing that the key to understanding the evolution of organisms lay largely in understanding the process by which they develop.

Developmental biology was already a major field of research with a lot of very able people in it. But because none of them seemed to think it had anything to do with evolution, they weren't doing the sorts of experiments that were needed to contribute to our understanding of evolution. So Mae-Wan decided to become a developmental biologist and do the relevant experiments herself.

In particular she was interested in phenocopies, cases in which if you interfere with the development of an organism you can produce varieties some of which occur naturally as mutants. Butterfly collectors know, for example, that if you can't collect a complete set of variants of a particular species, you can often get the missing ones by chilling the pupae of normal ones. They consider it cheating, by the way.

But the phenomenon tells us something important, that the variant form, like all form, is created not by the gene but by the developmental process which is capable of producing that form if it is suitably triggered either by the presence of a mutant gene or by some environmental perturbation. The conventional theory says we should concentrate on the trigger, rather than the creator of the form.

For neo-Darwinists, the developmental process follows a blueprint laid down in the DNA. The properties of the process itself have no influence on the outcome. We may say that for neo-Darwinists, developmental biology is the study of construction. On the epigenetic view it is also the study of architecture and design.

The 1979 paper, like the book we edited 5 years later, was not greeted with acclaim by the evolution community, far from it. The reviews of the book were almost uniformly hostile, and at last year's evolution meeting at the Royal Society, one speaker – who I think had been invited specifically to put the case for the conventional approach – still felt the need to be rude about a book published over 30 years ago. Mind you, in conversation I also discovered that quite a few of the audience had read it and took a different view.

You might think that things have changed. There is a lot of interest in epigenetics these days, but it's not what we had in mind. It turns out that the word has two meanings, and they are very different.

When Waddington coined the word epigenetics he meant everything that happens between genome and phenotype. But there is a second and much narrower definition, and that is the one that almost all biologists use today. There are a number of slightly different versions, but a typical statement is that epigenetics is "the study of heritable changes that do not involve changes to the DNA sequence." Heritable, by the way, here means passed on to other cells during development, not necessarily inherited from generation to generation, though of course they might be.

What is new about this work is that it gives prominence to the role of gene expression rather than concentrating only on the genes themselves. This is clearly a step forward, and it is yielding a better understanding of heredity and also of the early stages of development. It acknowledges that the environment has a much greater influence than the conventional theory allows. It seems to have removed the taboo on the inheritance of acquired characters. But it's still all about the genome.

There is also a definite downside to this activity. Sometimes in science an idea appears and for some reason doesn't catch on and is lost. Think of particulate inheritance which was discussed by Lucretius in 55BC but had to be discovered independently by Mendel almost two millennia later. That could happen here, because all the interest in the narrow definition may cover up the broader meaning that Waddington gave it and, with it, the ideas that he was advocating and that we put forward in the 1979 paper.

It's made worse by the way that the proponents of what they might call an epigenetic approach often actually mention that the word is due to Waddington but misquote him so that it appears it was their version he had in mind.

I don't suppose they do this deliberately; I'm sure it's an honest misunderstanding. It looks like one or two writers originally got it wrong and, as can happen in science and elsewhere, everybody else copies them instead of checking what Waddington actually wrote. But it may hold up progress because unless they actually go back to his work, or to what Mae-Wan and I did, people will assume they are taking from him all that he had to offer and the rest – the really important bit – will be lost.

(Curiously, much the same is happening to another of Waddington's contributions, the epigenetic landscape. It's actually an interesting mathematical model but it is now seen as merely a picture.)

Why does it matter which definition of epigenetics we use? The answer is that it makes a big difference to the study of evolution. The synthetic theory, or neo-Darwinism, is based on a very simple idea, natural selection acting on random variations caused by random mutations in genes. It is assumed that there is a 1-1 relationship between genotype and phenotype, or as biologists would say, one gene/one character.

Of course if you ask a biologist whether or not he believes in one gene/one character, he will assure you that he most certainly does not. No one could believe such a thing. There are multigene effects, regulatory genes, pleiotropy (one gene affecting more than one trait) and so on. Yet when you look at neo-Darwinist arguments you find that they depend implicitly on the assumption that it is one gene/one character or something very much like it.

There's a point here that mathematicians will be familiar with but others may not. In any theoretical discussion we start from assumptions. Axioms, or at least things that we accept as the case for the time being. But there are two kinds of assumptions, those that we make explicitly and acknowledge openly and those that we make implicitly, that we ourselves may not realise we are making. It's no use denying you believe in one gene/one character if it turns out that the work you do actually depends on it.

As George Bernard Shaw wrote in *Man and Superman*, "What a man believes may be ascertained not from his creed, but from the assumptions on which he habitually acts."

I obviously don't have time to discuss in any detail why I think we have to abandon the gene- or even genome-centred view of evolution. That would be a long talk all on its own. The example I gave of the explanation of form will have to do for now.

But there are at least three ways in which it matters.

First, it is important that scientists should study evolution in the most effective way. That's obvious, of course, but it still has to be said. Don't waste your time inventing *Just So* stories where there is real work to be done.

Second, neo-Darwinism has had a major influence on other subjects. The most obvious is evolutionary psychology. In the volume that is the founding text of the subject, we read not only of genes that make men prefer younger women and women prefer older men but also genes that make parents teach their children to have those preferences. Can we really believe such genes exist? I find it hard to credit, but can we expect others not to skip over the hard bits of such arguments when they see biologists, who should know about these things, happy to do just that?

It's not just where genes are involved, either. Just as Newtonian mechanics led people to see everything as a machine, so Darwinism leads us to the idea that to understand something we study not the thing itself but the external forces that act on it. One example is neo-classical economics, which is based on equilibrium arguments with the market playing the role that natural selection does in neo-Darwinism. There is an interesting article about this by the economist Paul Krugman, though he sees the parallel as a strength rather than a weakness of his subject.

Third, a good theory leads us to do important work. Her work on evolution led Mae-Wan to study developmental biology and make the discovery that led to *The Rainbow and the Worm* and the remarkable pictures that you will see later today. This led her to liquid crystals and the importance of physics in biology. And then to quantum mechanics and finally, as she became more and more convinced that what happens in organisms is related to fundamental processes in physics, to the whole question of the nature of space time.

Mae-Wan believed that the world is profoundly interconnected; that's a lot of why she found coherence and entanglement so fascinating. She also believed that the study of the world had to be interconnected. We must not try to study biology as a subject on its own with physics and chemistry allocated only bit parts. We should not set out to explain the whole of the living world in terms of a theory that can be stated in a couple of sentences. She worked in so many fields not on a whim or out of a desire for novelty but because what she learned in one always left her with important questions that could not be answered within that field itself.

And it's not just about science. Mae-Wan always insisted that interconnectedness does not end at the door of the laboratory. We cannot separate science from everything else we do as human beings. We must not work in science without considering how what we are doing affects humanity. We cannot do our best for humanity if we ignore what the best science has to tell us. That's why however well her pure scientific research was going, she was never tempted to give up ISIS and the work she was doing for the broader world.

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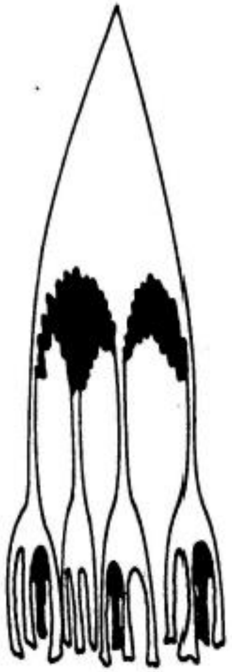

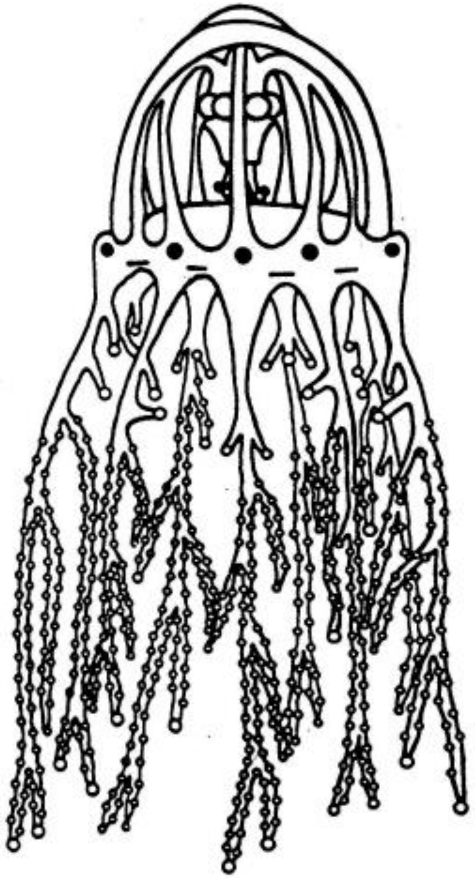

Homunculus

Se la fonte di vita chiusa in unampolla di vetro sigillata ermeticamente, viene seppellita per quaranta giorni in letame di cavallo e opportunamente magnetizzata comincia a muoversi e a prendere vita.

Dopo il tempo prescritto assume forma e somiglianza di essere umano, ma sarà trasparente e senza corpo fisico.
Nutrito artificialmente con arcanum sanguinis hominis per quaranta settimane e mantenuto a temperatura costante prenderà l aspetto di un bambino umano.

Chiameremo un tale essere Homunculus e pu   essere istruito ed allevato come ogni altro bambino fino all età adulta, quando otterrà giudizio ed intelletto.

“What a man believes may be ascertained not from his creed,
but from the assumptions on which he habitually acts.”

George Bernard Shaw: Man and Superman