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Q & A

Bill Martin

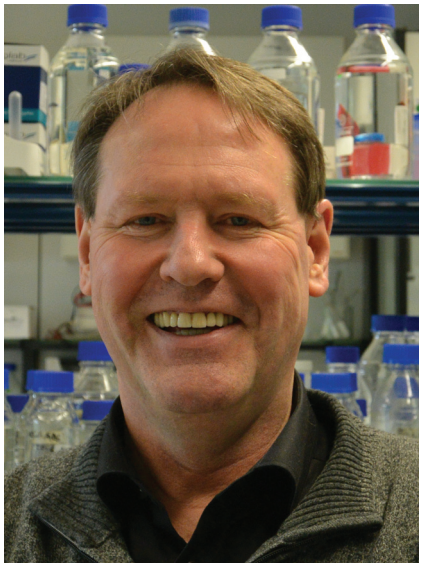
Bill Martin studied biology at Texas A&M and the University of Hannover. He did his PhD at the Max-Planck Institute for Breeding Research in Cologne under the generous supervision of Heinz Saedler, who discovered the transposons known as IS elements. After finishing his PhD in 1988, he did his postdoctoral work on chloroplast-cytosol isoenzymes, endosymbiosis, and gene transfer at the University of Braunschweig. In 1999, he received a full professorship at the University of Düsseldorf. His current interests are endosymbiosis, early evolution, and the origin of life.

What turned you on to biology in the first place? During my schooldays, I spent summers working in a garden shop. There was often an ornamental in the store called *Calathea lancifolia*, with long leaves that present the pattern of smaller, dark green leaves emerging from the midrib before the lighter green background of the leaf's surface. I assume it is based on chlorophyll content or plastid numbers. I would stare at that plant and wonder how the heck (and why) something like that could come to be. I still wonder. Today I call things like that a biological phenomenon; it's the kind of fascinating stuff that makes great research projects. I ended up going to college to learn more about plants so that I could have my own garden shop someday. Later I discovered that in order to have a garden shop, you need to study business, not biology.

Who were your key early influences? Though I did not know it then, in 1978 my microbiology teacher, Willard Taber (*The Impact of Fungi on Man*), said three things that set my course. The first thing was "We used to make insulin from pig pancreas, now we can put the gene into *E. coli* and make it in buckets". Hmm, I thought, gene technology, what an advance. The second thing was "A theory combines mutually consistent hypotheses. Every observation for which the theory cannot account adds weight in the form of corollary assumptions. When a new theory comes along that requires fewer corollary assumptions to account for the same or more observations, it replaces the old one". Ah, I thought, so that's how science works. The third thing he said was "And some people think that chloroplasts used to be free-living cyanobacteria". Wow, I thought. Endosymbiosis — that's really interesting. I want to know more.

And what drew you to your specific field of research? Excellent chemistry teachers in college (Shapiro, Berthold, Habermehl), plus burning curiosity for the question of how life works and how that came to be.

What is the best advice you've been given? When I was ready to do my undergraduate thesis at the University of Hannover in 1984, I knew that I wanted to do something that had to do with plants, but there were several professors and I did not know whom to approach. A highly respected postdoc in the Institute of Botany, Hartmut Heinze, suggested that I ask Rüdiger Cerff whether he would be willing to take on a new student. I had not heard Rüdiger's lectures and did not know what his research was all about. I took Hartmut's advice and asked Rüdiger if there was work to do. Rüdiger had spent years in the cold room to isolate the chloroplast and cytosol isoenzymes for glyceraldehyde-3-phosphate dehydrogenase from mustard seedlings. It turned out that chloroplast and cytosol isoenzymes like those for GAPDH were really important for endosymbiotic theory. Ah, endosymbiosis. Rüdiger knew from genetics that both enzymes were nuclear encoded. He also knew that the chloroplast enzyme shared properties with the enzymes from bacteria, so there was a good chance that the gene for the chloroplast enzyme had been acquired from the cyanobacterial ancestor of plastids. My thesis was to construct and isolate cDNA clones for both enzymes using antisera, which Rüdiger had generated against the purified enzymes, via a technique called hybrid release translation. Then I was to sequence them with Walter Gilbert's chemical method. It was an exciting time. It worked; the chloroplast enzyme did indeed appear to have been transferred from the endosymbiont to



the nucleus. We finally got the paper published in 1986, and I have been working on endosymbiosis, gene transfer and early evolution in one way or another ever since.

As an unexpected observation during that work, the gene for cytosolic GAPDH also appeared to have undergone lateral gene transfer (LGT) during evolution, we reported; though we, like others after us, initially got the direction of transfer wrong. It didn't take too long until endosymbiotic gene transfer and lateral gene transfer became very popular in molecular evolution circles. In some ways too popular, it might seem. By 'too popular' I mean that there soon followed a time, continuing to today, where people who compare sequences interpreted every odd branch in each tree they constructed, or every unexpected gene in each eukaryotic genome they assembled, as evidence for LGT in eukaryotes (note: eukaryotes recombine via sex, not LGT). That generated a kind of a market for increasingly sensational claims for 'incredible' LGT, for example, claims that genes have been transferred from one eukaryote to another by meteorites as vectors, or claims that eukaryote genomes can consist of up to 17% of recently acquired foreign DNA.

Such claims do not square off well with what we know from genetics. People became uncritical and went overboard with LGT. There is a difference between trying to understand

something about nature and trying to get sensational claims published. For bacterial geneticists, LGT was never new. But for molecular evolutionists, who were doing trees to retrace life's genealogy, LGT appeared as something both new, exciting and hotly marketable it would seem. One might say that our GAPDH paper was a pebble of LGT that kicked loose quite a few other pebbles on its way down the mountain, as Russ Doolittle, Ford Doolittle and their buddies might recall. Gene trees have inherent error, and most LGT-like patterns in eukaryotes, we now see, are best explained as the result of differential loss.

Do you have a scientific hero? Several, I suppose, and I have had the great fortune to publish with some of them. Miklos Müller discovered hydrogenosomes and worked on them diligently for decades to try to understand how eukaryotic anaerobes work. Nothing he found fit properly into the existing schemes. But he plowed forward, holding onto the observations. Now we know that hydrogenosomes are central to understanding the evolution of eukaryote physiology. John Baross immediately recognized how important hydrothermal vents are for understanding life's origin. His ideas were not popular, but they have proven to be very robust. Same is true for Mike Russell, who immediately appreciated how the naturally chemiosmotic nature of alkaline hydrothermal vents provided links to life. Rolf Thauer, Georg Fuchs and Wolfgang Buckel figured out the general reaction mechanism of how life works for some seemingly simple anaerobes, microbes that turned out to be not so simple after all — that's quite an advance in understanding life. Harald Morowitz, who passed away in March of this year, contended 60 years ago that life needs to be seen in light of thermodynamics. Was he ever right. Masatoshi Nei brought the concept of distance to evolution and underscored the role of mutation. Margaret Dayhoff established all of the principles underlying protein sequence comparison and invented bioinformatics. They are all heros for me.

Do you have a favourite paper or science book? My favourite paper is probably Mereschkowsky's 1905 paper about the origin of plastids. He called it symbiogenesis; today we call it endosymbiosis. Klaus Kowallik and I translated that paper into English a few years back. Mereschkowsky was clearly aware that he had made a very big leap in understanding the origin of photosynthesis in eukaryotes. It is a very exciting paper. Eck and Dayhoff 1966 is right up there: physiology, evolution, structure, iron sulfur, redox chemistry, gene duplication, sequence conservation, a full service paper. Dayhoff *et al*. 1964 is rising rapidly in my charts, though, too. It was an early stab at charting out the speciation of carbon on the primitive earth with the goal of understanding life's origin, way ahead of its time. My favourite science book would be *Brock Microbiology*, although one cannot get enough of Nick Lane's recent books.

Do you think there is too much emphasis on big data-gathering collaborations as opposed to hypothesis-driven research by small groups? Data gathering is important, as long as the data are useful and relevant. There is a lot to be said for just going out and collecting important observations (discovery) without having a specific hypothesis to test. For example, in the 1960s, biologists were using electron microscopes to get the first glimpses of cells and the fine details of their inner structure. There was no hypothesis behind discovering what cells look like under the electron microscope. The more important distinction is, in my view, not whether science is hypothesis-driven or not, but whether science is done in big collaborations or by individuals. Big collaborations tend to produce science by committee, where everyone is a little bit right. That is not how bona fide scientific progress is achieved. Many major advances in our understanding of biology are the result of one individual's curiosity for a particular phenomenon. Barbara McClintock and transposable elements is a classic example. She made great observations from which she developed a hypothesis to account for them.

John F. Allen explained to me the significance of scientific hypotheses using the example of Peter Mitchell, who achieved a huge scientific advance by just thinking about a very hard problem, conceptually cracking it open, and then providing the evidence. While experts were trying (in vain it would turn out) to identify a mechanism of substrate level phosphorylation in mitochondria, Mitchell posited out of the blue in 1961 that mitochondria synthesize ATP by coupling the redox reactions of pyruvate oxidation to the generation of proton gradients across the inner mitochondrial membrane and then harnessing that ion gradient to phosphorylate ADP via a hypothetical coupling factor, a complex which we today call the rotor stator ATP synthase. He called the mechanism chemiosmotic. It was just an idea, the result of thinking about a problem. People laughed at him for about a decade, until it became undeniable that his inference was completely right, to the letter. Breathtaking.

If you had not made it as a scientist, what would you have become? A carpenter.

If you had to choose a different field, what would it be? Geochemistry. There are two main ways to study early evolution: through genes and through the geochemical record. In that endeavour, life science and Earth science share some of the same problems. In genomes, we have abundant data about early evolution, but it is not always obvious how to extract that evolutionary information from the observation (genome sequence). We need models of various sorts (and computers) to distill a handful of evolutionary insights from thousands of genomes and trillions of bases. The geochemists looking at early evolution are faced with similar problems. They have trillions of rocks that can be dated using various techniques. The rocks and minerals contain information about early Earth and life processes, but in order to extract that information, various sorts of models are needed to generate expectations under different scenarios. Old rocks can be quite exciting in that respect. But both in biology and geology, if the models are off target, so are the inferences. That keeps the suspense up.

Which aspect of science would you wish the general public knew more about? How subjective the scientific process really is and why people who

seek power and influence should be in politics, not science.

Is there a scientific idea/concept/hypothesis that you wish didn't exist? How much space do I have here?

What's your favourite experiment? Linus Pauling investigated the crystal structure of small peptides that he synthesized. From that and from his exact measurements of bond lengths in amino acids, he brought the concepts of alpha helices and beta sheets to science. Not bad. We have not found anything beyond that yet. Anfinsens's conclusion from scrambled RNase that the information needed for the proper folding of a polypeptide is contained within the amino acid sequence is a brilliant logical inference.

Which historical scientist would you like to meet and what would you ask her/him? Margaret Dayhoff, and I would ask her "Is there anything I can do to help you?"

Is there enough left to discover? Oh come on. If you had asked me 30 years ago, I would have said, "Hey, we have replaced the slide rule with affordable pocket calculators and we have fax machines. Can't top that, though colour will surely come someday, like with TVs." In 30 years from now, maybe the internet or its descendants will know, roughly, how the patterns in the leaves of *Calathea* came to be during evolution. Maybe we will even know where else in our solar system nature took steps towards life.

What's the single most important thing that you have come to realize about nature? Life is an exergonic chemical reaction. It's the energy releasing redox reaction at the core of metabolism that makes life run, and throughout all of life's history it is one and the same reaction that has been running in uninterrupted continuity from life's onset. Everything else is secondary, manifestations of what is possible when the energy is harnessed to make genes that pass the torch.

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Quick guide

Colour polymorphism

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What is colour polymorphism? Colour polymorphism refers to the occurrence of multiple discrete colour phenotypes within populations that result directly from genetic variation. Direct genetic causality distinguishes colour polymorphism from polyphenism, whereby identical genotypes possess the ability to express varied phenotypes depending upon the environment. This definition also excludes ontogenetic and reversible colour change. Colour polymorphism may be limited to the presence of just two discrete morphs (dichromatism). Cases involving multiple morphs are not uncommon, however, and are particularly well documented for colour polymorphism. Dramatic examples include the exuberantly polymorphic happy-face spider (*Theridion grallator*) that exhibits 12 different morphs across four Hawaiian islands, or poison strawberry frogs (*Oophaga pumilio*) with at least 20 true-breeding morphs across their Central American distribution (Figure 1).

How does colour polymorphism develop? Colour in nature is almost exclusively due to pigments that absorb light or physical structures that reflect it. Both properties may be highly sensitive to genetic variation. In some cases, starkly divergent colour patterns may result from allelic variation in one or a few genes. Cichlid fish of the genus *Amphilophus*, for example, exhibit a dark-versus-gold polymorphism that is entirely due to alleles at a single pigment-controlling locus. Likewise, human eye colour is largely determined by the outcome of dominant and epistatic allelic interactions at two primary loci. In more complex cases, polymorphisms may result from variation across multiple genes that segregate together. This linkage across loci can enable discrete yet highly complex colour phenotypes while precluding less fit intermediates.

Is colour polymorphism common? Colour polymorphism occurs across a breadth of taxa and ecological contexts. Cases are documented for most major metazoan animal groups (Figure 1), across gymnosperm and angiosperm plants, and for species residing in terrestrial and aquatic habitats. Among animals, the incidence of colour polymorphism appears over-represented (if not over-reported) in taxa such as birds, anurans and lepidopterans. Functionally, polymorphism has been documented for colour traits involved in sexual signalling, crypsis, thermoregulation, mutualism, aposematism and in various forms of deceptive signaling including Batesian and Müllerian mimicry.

How is colour polymorphism maintained? Stable polymorphism is thought to require some form of balancing selection to maintain equivalent average fitness among colour morphs. One obvious candidate is negative frequency-dependent selection, which arises when rarity confers a selective advantage. This is particularly well established in the context of predation, as in the classic case of polymorphic grove snails (Figure 1C,D), and is referred to as 'apostatic selection'. Visually guided predators, such as birds, often memorize and form 'search images' of locally abundant prey. Rare prey morphs therefore benefit from reduced recognition and hence suffer less predation, up until the point at which they become the more common variety. The predators' search image is then switched to the newly abundant morph, and the cycle begins again.

Other examples for negative frequency-dependent selection come from sexual competition. Mate choice, for example, may levy selection of this nature by favouring novel or rare colour phenotypes, as hypothesized for male guppies. For intra-sexual selection, a notable example is the side-blotched lizard *Uta stansburiana*. Males of this species exhibit three throat-colour morphs — blue, orange and yellow — that signal distinct male-competitive strategies.