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or so members, created with this aim in mind. The result was an invitation to the first Pugwash Conference on Science and World Affairs in Nova Scotia in 1957, and a visit to Moscow (the first of 22) the following year. This in turn led to his appointment to President Eisenhower’s scientific advisory committee on nuclear arms control, and thence to those of Kennedy, Nixon and Carter. Doty made firm friends in Russia with the likes of Kapitza and Sakharov, and these ties developed into an informal, but influential ‘Track II diplomacy’ channel.

Such activities left him all too little time for the lab. He contrived to remain active in the affairs of Harvard: he was deeply involved in plans to overhaul the education system, raised support for the creation of a new Department of Biochemistry and Molecular Biology, and became its first chairman. His eye for talent was unerring, and he had always been active in the recruiting of new faculty, most famously, Jim Watson. The new Department — ‘Camelot’ to one of its most distinguished members, Matthew Meselson — thrived bounteously. Doty even continued to deliver at least some of the lectures in his course on macromolecules, although most he left to his students and postdocs. I recall one late arrival in the lecture-hall, when he disarmed the restive audience by announcing that he thought it better to come late than unprepared. His research students were often fractious, unable, they said, to understand why saving civilization from a nuclear holocaust should take precedence over research on DNA. Doty had in fact imparted momentum to the flywheel, which continued for a good while to revolve in his absence. There were useful contributions to understanding the genetic code, to determining the direction of transcription, and later still there was an incisive study of the effects of mismatches in DNA sequence. All the same, the lustre of the laboratory was fading. Good students, postdocs and foreign visitors still came, and many lesser institutions might have been well pleased with the output, but Doty could not have been altogether content. His devotion to science was not extinguished; when one managed to secure a precious half-hour with him to discuss data he still displayed his preternatural quickness of grasp, and in an instant he could have leapt ahead of one’s own sluggish ruminations.

Yet the allure of national and world affairs was too strong to be resisted. Henry Kissinger maintained that his bruising experiences on the Harvard Faculty had equipped him to confront hostile world powers with equanimity. The desire to exercise their high intelligence in a wider sphere has always afflicted top academics. There can be no doubting Doty’s passion and commitment to nuclear disarmament, and to better international understanding generally, nor of the magnitude of his achievements. But Helga Doty, who wanted to keep him in the lab, was heard to say of her husband, ‘Washington is heady wine to Paul’. In any event, it was some years before he finally decided to shut up shop and devote himself entirely to the Belfer Center for Science and International Affairs. He had founded this organization (now subsumed within the Kennedy School of Government) in 1974 with the support of McGeorge Bundy, President of the Ford Foundation, previously National Security Adviser to two presidents, and by no means a natural political ally. It was a tribute to Doty’s powers of persuasion. Amongst the alumni nurtured by Doty are several members of the Obama administration.

Doty was a large man. I remember him as a genial blond Buddha. With his unmistakable well-modulated tenor voice, he was an impressive performer on the lecture podium, lucid, amusing and direct. His writing was a model of clarity and precision, all the more astonishing in that he should have been a confessed dyslexic. He took pride in the successes of his students, and indeed his record is remarkable: among his academic progeny are fourteen members of the National Academy of Sciences, one indeed a President. At a gathering last year to mark his 90th birthday he appeared in his motorized wheelchair, astonishingly unchanged in appearance, his memory and intellectual acuity seemingly undimmed. He chose the moment of his death, in control to the last. Helga Doty died in 2004. He leaves a son from his first marriage, which ended in divorce, and three daughters by Helga.

King’s College, Randall Division of Cell and Molecular Biophysics, Guy’s Campus, London SE1 1UL, UK.
E-mail: walter.gratzer@gmail.com

Q & A

John A. Endler

John A. Endler is a Professor of Sensory Ecology and Evolution at Deakin University and an Adjunct professor of Zoology at James Cook University, both in Australia. He regards himself as a 19th century natural historian who uses 21st century techniques to answer questions generated originally from field observations. His research is in the area of overlap among Evolutionary Biology, Sensory Ecology, Behavioural Ecology, Animal Behaviour, Neuroethology and Biophysics. He enjoys combining field work, field experiments, lab work, and theoretical methods as well as constructing electromechanical-optical equipment and software for himself and students.

Did you always want to be a biologist?
Yes, and apparently I was asking detailed questions about animals and plants when I was four. I suppose others were the same way, but I am very happy that I did not ‘outgrow’ my curiosity! Curiosity about how the world works is the ultimate source of genuinely new hypotheses, and I cannot think of a single major discovery in any branch of science that did not start out as a curious question rather than an attempt to solve an applied problem. I much prefer attempting to satisfy my unabashed curiosity about unexplored areas of biology to working in the intellectual suburbs.

Who has influenced you the most?
I don’t know where my original interest in biology and science came from because both my parents were musicians, but at least they encouraged my curiosity. Park rangers (this was before they all had to become policemen and PR experts) and museums helped too. I simply find animals and plants fascinating. As an undergraduate, Robert C. Stebbins of UC Berkeley encouraged my interest in accurate and careful natural history observations and asking questions about what I observed. Perhaps the two strongest influences on my intellectual development were Ernst Mayr and Erle Stanley Gardner (creator of the fictional character Perry Mason). I loved Mayr’s careful logical
arguments with loads of evidence from multiple fields, and Perry Mason’s insistence upon considering alternative hypotheses and getting at the truth regardless of what was commonly assumed.

It is a pity I never met either of these people. Mayr was always out of town when I visited Harvard; late in his life, Mayr finally said that he wasn’t actually avoiding me, although I had my doubts because my book Geographic Variation, Speciation and Clines (1977) used Perry Mason methods to squash Mayr’s idea that the only form of speciation is allopatric. Instead of attacking my ideas in that book (in which I talked about parapatric speciation), like he did with other ideas he disagreed with, he invented the similar-sounding peripatric speciation. The lack of attack and redirection I regard as an admission that I was right. It’s rather like two competing cats who face off by carefully looking away. I’ve always thought that this was a pity because I really respected him, and still wish I could have had a good science discussion with him.

My Ph.D. supervisor, Bryan Clarke, was fantastic in honing my logical skills in forming and testing hypothesis, and I cannot think of a better possible supervisor than him. I try to be like him to my own students.

What do you think is your most interesting work? My first work demonstrated that significant genetically-determined geographical differentiation can occur in spite of gene flow (genetic mixing) among populations, and that this can lead to speciation, contrary to the opinion at that time. This led me to want to know what causes divergence among populations, and thus to my survey of natural selection which showed that it is commonly quite strong in nature, contrary to the opinion at the time. In turn, this led me to work on natural populations of guppies which had known predation gradients, and I was able to show that the colour patterns in different places represent a local balance between predation and sexual selection. Work done with a star student and later collaborator, David Reznick, demonstrated the effects of locally varying predation on life-history pattern divergence.

The next logical step was my exploration of what makes some colour patterns more conspicuous than others. To do this I combined evolution with sensory physiology to make predictions about the joint evolution of signals, signal-based choice behavior, and sensory systems. The network of functional and selective processes I called ‘sensory drive’, and it allows testable predictions about the direction of evolution as well as the strength of natural selection, from first principles.

After spending a long time with the sensory ecology of colour I decided to explore other aspects of sensory drive, notably the interaction between colour pattern and geometry. My most recent discovery is that Great Bowerbirds construct and maintain forced perspective and other visual illusions which affect mating success, and that any illusion produced by a male which captures a female’s attention could increase the time she assesses him, possibly leading to increased mating success, even though it does not necessarily signal male quality. The common theme in my research has always been: why do animals look the way they do; what causes biodiversity?

Where do you get all your ideas? From careful observation of species in natural habitats and constantly asking ‘why’ about anything I see. I started a postdoc with Robert MacArthur, but he died a third through my time at Princeton. He was also an enthusiastic natural historian and he told me that he also got all his ideas from natural history and asking ‘why’. This encouraged me to continue in this way. I always tell my students that they cannot become a creative original scientist unless they become a ‘why monster’, as I have been called (affectionately) by some of my students. Once one starts observing species in their natural habitats the number of questions increases exponentially as more and more questions lead to still more, and many (not all!) are testable. I get so many ideas that I constantly give them to students and peers and then forget about them (the ideas, not the colleagues); when someone presents me with a study and I say that I really like it, many times I’m told it was actually my idea originally. Slightly embarrassing, but it’s good to help others to advance science.

Why have you moved universities so often? There are several reasons. First, I really enjoy the stimulation of new colleagues, new and different ways of doing science, and students with new backgrounds. It also gives me the chance of living in and near different habitats. This is the best way to retain a global rather than a local perspective. Second, changing universities comes with set-up costs which are not tied to a predetermined project. Every time I have moved I have been able to add very new and original scientific problems which could not possibly be supported by regular granting agencies (which have difficulty justifying spending their money on so called ‘high-risk’ projects). Set-up costs allow genuinely innovative work. Third, I move when the administrative burden becomes excessive. I’m really only interested in doing and discussing science, and teaching students about it and how to do it. I find other aspects of academic life intensely boring if not repugnant.

What is the best advice you’ve been given? The best advice was given to me by my then Ph.D. supervisor, Bryan C. Clarke: “Always ask yourself ‘what is the minimum critical evidence needed to make my point unequivocally and clearly?’”. This applies not only to writing a paper but also to experimental design and, to a lesser extent, an entire research program. It’s a great way to focus on what is important and relevant. It also helps in being an editor or reviewer.

What advice would you offer someone who is starting a career in biology? First, never hesitate to ask questions about science to people whom you don’t know (email or in person in meetings). When I was a Ph.D. student I noticed that some people were very helpful and others either didn’t reply or were superficial. However, I noticed that the people who were not helpful also tended to produce the poorest papers, and when I asked my Ph.D supervisor about this, he said that he was glad I noticed and he observed it too. It seems that only second-rate scientists are unhelpful, probably because they are afraid of being ‘shown up’. So don’t hesitate to ask, anyone. But be considerate; think about your question as much as possible before asking someone (even your own supervisor). And don’t despair if you don’t get an answer for a week, the best scientists are often the busiest.

My basic advice for your career is to never forget why you went into biology
to begin with and be bloody-minded about continuing this specific interest. You should always enjoy biology, even when some aspects of doing research are tedious or even unsuccessful. If you don’t enjoy what you are doing, then you might as well be in business and be paid well to do boring things! Beyond that it is a matter of personal style; my advice depends upon where you are on the personality gradient between risk-adverse and risk-prone, and how comfortable you are with the unpredictable.

At one extreme, if you are (like me) more risk-prone, you should be extremely exploratory, daring, and original in the scientific questions you ask and do research on. Do ‘interesting’ science rather than ‘important’ science. This is more likely to yield significant new discoveries because few people have addressed supposedly ‘unimportant’ questions. The history of science suggests that almost no major discoveries were done because that research topic was ‘important’ at that time. There is a bigger risk to your career in going for interesting science for three reasons: you might get into an intellectual cul-de-sac, so you need to learn how to recognize dead ends; it is much harder to get funding for really original or ‘unimportant’ science; you need to have thorough knowledge which cuts across several scientific fields, which takes longer and requires more effort. You will also have to learn how to recognize completely new phenomena. Don’t get caught in intellectual ruts caused by excessive reading of the literature, but do be careful to ensure that you give all credit to all published work. Let natural phenomena be your guide rather than the literature if you want to make really new discoveries.

At the other extreme, if you are risk-adverse, then stick to ‘important’ and applied science or technology, it is far easier because questions are well-defined and funding is easy, and its easy to churn out papers making tiny advances, so your career will advance quickly. But the risk is that you won’t make any significant contribution to science and your name will be forgotten after you go into administration because tiny advances are not satisfying, or retire, rich. As you can see, where you sit on the gradient is a matter of taste and style, but don’t forget your original goals!

What do you think of the worldwide trend in research councils and foundations towards more and more applied research at the expense of ‘pure’ research? I am worried by this trend. It is presumably driven by the fact that research councils and foundations have to justify spending money to their governments and boards, and it is difficult to sustain funding if it seems ‘unimportant’ or even ‘useless’. Very few people controlling research funding realize that breakthroughs in science are like a tree giving off thousands of seeds of which only a few germinate. As a result, the people in councils have to favor ‘important’ science, and researchers have to stretch descriptions of basic research to sound as though it has significant applied implications.

This is terrible, for two reasons. First it inhibits genuine exploratory (‘blue sky’) research, hence greatly reduces the probability of genuinely new discoveries and concepts. Second, and positively dangerous, the constant exaggerated description of all research projects having supposedly significant applied outcomes is constantly raising the expectations of the public. As this gets worse and worse expectations rise and failures become more frequent, and public confidence in science declines. This is the classical problem of short-term gains at the expense of long-term survival. Pretending all science has immediate beneficial applications results in long term destruction of support for and interest in science. Right now we are just depending upon sheer numbers of researchers stumbling on new phenomena in a social atmosphere of rapidly declining confidence in science because we are constantly raising expectations. Somebody needs to write a popular book about the cultural/social environment that has favored major scientific breakthroughs in the past, and how this needs to be encouraged. We risk the long-term survival of science by not letting the public know how science really proceeds.

If you were to start over, would you do it again? Yes! I really enjoy doing science, satisfying my curiosity and discovering the unexpected.

Centre for Integrative Ecology, School of Life an Environmental Sciences, Deakin University at Waurn Ponds, Piddons Road, Geelong, Victoria 3217, Australia.
E-mail: John.Endler@deakin.edu.au

Quick guides

Oncogene addiction

Jeffrey Settleman

What is oncogene addiction? The term ‘oncogene addiction’ was first coined by Bernard Weinstein to describe the dependency of certain tumor cells on a single activated oncogenic protein or pathway to maintain their malignant properties, despite the likely accumulation of multiple gain- and loss-of-function mutations that contribute to tumorigenesis. The term has been reinforced by several reported findings in animal tumor models in which oncogene-driven tumors, either generated as xenografts or through the use of genetically engineered models, have been found to undergo regression, associated with proliferative arrest, apoptosis, and/or differentiation following the acute inhibition of oncoprotein function.

Should this surprise anyone? Many scientists in the oncology research community view the oncogene addiction concept as ‘trivial’, suggesting that it is obvious that a mutation that contributes causally to tumorigenesis would be required for cancer cells to maintain their malignant phenotype. However, this is almost certainly not universally true. Thus, cancer cells frequently undergo genome instability caused by disruption of normal DNA repair and replication mechanisms, and this can certainly result from mutational events that affect, for example, genes encoding components of the DNA damage response machinery. Such mutational events lead to the accumulation of additional potentially oncogenic mutations, but are clearly exerting their actions via a ‘hit and run’ mechanism. Similarly, one could imagine oncogenic events that play a role in the initiation of tumorigenesis, for example, by expanding a tumor stem cell population, but that are not necessarily required to maintain tumorigenicity once a tumor has sufficiently ‘matured’.

What is the ‘oncogenic shock’ theory? Oncogenic shock is a signaling mechanism that has been proposed