The Phenotypic Expression of a Genotype: Bringing Muddy Boots and Micropipettes Together

Roger Hull

Emeritus Fellow, John Innes Center, Norwich Research Park, Colney, Norwich NR4 7UH, United Kingdom; email: Roger.hull@bbsrc.ac.uk

Annu. Rev. Phytopathol. 2008. 46:1–11

First published online as a Review in Advance on May 28, 2008

The *Annual Review of Phytopathology* is online at phyto.annualreviews.org

This article's doi: 10.1146/annurev.phyto.46.110807.094143

0066-4286/08/0908/0001$20.00

Key Words

virus epidemiology, virus characterization, molecular biology, *Alfalfa mosaic virus*, *Cauliflower mosaic virus*, rice tungro viruses, *Banana streak virus*, developing countries

Abstract

Starting with the influences of having a father who was an agricultural plant pathologist, I sketch my career through university and research institute from field epidemiology, basic virus characterization to molecular biology. I note what I consider to be the highlights of my scientific career and the events that shaped the development of my thinking. These include secondment to teach in a university in Uganda, a sabbatical year in the University of California, Davis, where I became aware of the emerging DNA technology, studying the molecular biology of *Cauliflower mosaic virus*, rice tungro viruses, and *Banana streak virus* with the aim of developing diagnostics and approaches to control of viruses. Bringing these experiences together, I am now involved in facilitating the uptake of the application of biotechnology to crop improvement in developing countries. I conclude with some thoughts on opportunities for young plant pathologists over the next years of rapid change. As I am one of the few British scientists who have had the honor of writing such an article, I also note some of the vagaries of the British system.

THE BEGINNINGS

The invitation from the editor of *Annual Review of Phytopathology* to write this prefatory was a great surprise and is indeed an honor. The invitation asked me to reflect on my experiences as a plant pathologist and to discuss my professional views and history. As previous writers did, I have looked back through the prefaces over the past few years and find that there has only been one recently from the United Kingdom and that was a tribute in 1997 to Philip Gregory's contribution as a pioneer leader of phytopathology. Thus, part of this article will be to comment on the former British way of developing a scientific career. As well as describing what I have considered to be a satisfactory and rewarding career, I would also like to take this opportunity to discuss some views on what plant pathologists can offer to the increasing problems in developing countries.

My history is a good demonstration of the phenotypic expression of a genotype. My father, Raymond Hull, was a plant pathologist working on sugar beet and specialized on virus yellows of that crop. His first job after obtaining his PhD was as a plant pathologist with the Midland Agricultural College (now part of the University of Nottingham). He set up the lab in one room of his house in a small village near Lincoln (in the east of England) with a glasshouse in the garden. Thus, I grew up in a research environment with, as a small child, the special treat of visiting the lab and lighting the Bunsen burner! My father had strong connections with the virologists at Rothamsted Experimental Station and the story is recounted of a visit of some senior virologists from there—including Fred Bawden (Sir Frederick Bawden who became director of Rothamsted) and Marion Watson (who unveiled virus-vector relationships). The story is that I came across my father with his visitors in the glasshouse, locked the door, and threw the key into the water butt! The village where we lived was very feudal, and I helped with the harvest, milking cows, etc., giving me a good grounding in farming (at least the old way of doing it). In the late 1940s my father's unit became a substation of Rothamsted and eventually grew into Broom's Barn Experimental Station, the department of Rothamsted devoted to research on sugar beet. As a teenager, I did vacation jobs helping my father with harvesting and recording sugar-beet experiments and learning about scientific experimentation. Thus I grew up in an environment of agricultural research and plant pathology.

After high school and two years' compulsory military service I went to Cambridge University to read Natural Sciences. In the Natural Sciences tripos one studied three subjects for the first two years and then specialized in one subject for the third year. I read botany, zoology, and geology in Part 1, hoping to specialize in geology, but the geology professor dissuaded me, and several others, by saying that there were no job prospects in that field. So I read botany in Part 2, specializing in plant pathology under Dennis Garret. We were fortunate to have some (after lunch) lectures on plant viruses from Kenneth Smith, one of the doyens of plant virology. Three years later oil was discovered in the North Sea and there was a great demand for geologists; however, I still think that I made the right choice.

For postgraduate studies I had the offer of a position with Marion Watson at Rothamsted but thought that that was too incestuous. So I took a job as a demonstrator at Wye College, the agricultural college of the University of London, researching for a Ph.D. at the same time. The demonstrator job involved teaching botany and plant pathology in practical classes, but after a few weeks my professor said, "I think it would be good experience for you to give some lectures. Would you give five lectures to the second-year horticulture students on conifers starting in two weeks' time?" This led to much blood, sweat, and toil in preparation but was an invaluable experience. In those days, and even now, a Ph.D. in England was by research and did not involve any course work. For my research topic I was given the choice between studying the viruses of sweet peas (*Lathyrus odoratus*) or working on local lesion

production of *Tomato spotted wilt virus* (which was a rarity at that time). I chose the sweet peas and set up large experimental plots to study the epidemiology of the viruses as well as the effects of infection on the yield of flowers—obviously influenced by the experience of helping my father with his sugar beet experiments. The work involved daily observations on the plants for signs of infection and aphid vectors, identifying the viruses, aphid trapping, and counting the flower yield. For the latter I was very popular with the organizers of graduation ceremonies with requests for buckets full of flowers for the decorations. The field studies were done over three summers and the winters were spent identifying the viruses, analyzing results, etc. For virus identification the only techniques available were diagnostic hosts and serology. There were several potyviruses infecting the sweet peas and I tried to see if gel diffusion tests could be used for these rod-shaped viruses. I realized that the agar normally used for these tests was made up from agaropectin and agarose and that the fibrous nature of agaropectin would trap the virus particles. In those days agarose was not commercially available and so I had to make it from agar. At one stage this involved centrifuging at 10,000 rpm for 10 min at 50°C, which required putting the rotor in an oven and heating the centrifuge chamber with a hair dryer.

INTRODUCTION TO THE TROPICS

As I was finishing my Ph.D. my professor asked me if I would like to go to Makerere University, Kampala, Uganda to teach for six months. I checked with my wife whose reply was, "When do we leave?" A date was fixed and there was a frenetic final writing up of my thesis—in those days one had to type five carbon copies and, if a mistake was made, the page had to be started again. I finished typing the night before leaving for Uganda, gave it to my professor the next day to be bound ready for examination on my return, and took the flight to Uganda that night. Two days later I was teaching agricultural botany to African students, once again on a strong learning curve as I had never seen the crops we were dealing with before. I wanted to do some research out there and was introduced to staff at Kawanda Agricultural Research Station just outside Kampala. Groundnut rosette disease was causing great problems, and it was suggested that further epidemiological information was needed on it. So I set up a field plot to study the spread of the virus by its aphid vector, *Aphis craccivora*. This involved sitting on a stool in the plot (under an umbrella to protect me against the sun) and recording aphid landings on a quadrant of plants, as well as the conventional recording of first occurrence of disease, aphid numbers, etc. From these "mark-one eyeball" observations I developed the hypothesis of the spacing of plants and edge effect on aphid attraction to plants and published a paper in *Nature* (3). Although I did not realize it at the time, the six months in close contact with tropical agriculture and the problems in developing countries would affect my future career interests.

CAMBRIDGE AND THEN TO NORWICH

On return from Uganda and after obtaining my Ph.D., Wye College tried to keep me by offering a promotion. However, I felt that the demands of 70% teaching and 80% research were too great and so I looked for opportunities for a research career. I heard that Roy Markham had a research position in the Virus Research Unit (originally set up by Kenneth Smith) at Cambridge. I phoned him and he asked me to visit him the next morning. After I was shown round the Unit he asked, "When can you start?"—so different from the formal applications, short listing, interviews, etc., nowadays! So I moved to Cambridge and started work on fundamental studies of viruses using both biological and physical techniques. I went on another rapid learning curve from Roy and colleagues on physical techniques such as analytical ultracentrifugation (the Beckman Model E), diffusion (the Beckman Model H),

and electron microscopy. Initially, I started with groundnut rosette as I had brought material back from Uganda and found that the disease was caused by two viruses, *Groundnut rosette virus* and *Groundnut rosette assistor virus* (7). This work went well until there was a failure of the glasshouse heating on a very frosty night and all the plant material was lost.

In 1968 Roy Markham was appointed director of the John Innes Institute (JI) (now the John Innes Center), which had just moved to Norwich. The JI was founded in 1910 at Merton, South London, as an "institution for horticultural education," following the model of Rothamsted, which focused on agriculture. The first director was William Bateson, one of the rediscoverers of Mendel's work, who set the ethos of the institute for fundamental research on plants and microorganisms. Roy took the staff of the Virus Research Unit with him as a new virus department at JI and so I was able to continue fundamental studies on viruses. In collaboration with other colleagues, I started working on *Alfalfa mosaic virus* (AMV), doing much biophysical analysis and electron microscopy. I was fortunate to have access to Kennneth Smith's virus collection, which had been made over the previous three decades, and unearthed some interesting strains of the virus. One strain from New Zealand had unusually long particles that formed some very attractive aggregation in vivo (4), resembling frost patterns and making an interesting design for a Christmas card. Working with Kitty Plaskitt and Graham Hills, I made a study of the in vivo aggregation bodies of 24 strains of AMV and used 2 of them with distinct aggregation bodies to study cross protection within the cell (10). We showed that the protecting strain dominated first parts of the cell, then groups of cells, and finally the whole plant. Looking back, this 35-year-old work has implications important to the understanding of RNA silencing, so the message is to not neglect old-fashioned observations.

Around the time of the move from Cambridge, we were approached by Dr. Nayar from Bangalore, India to look at Sandal spike disease to establish whether it might have a viral etiology. Electron microscopy of thin sections of infected material showed large bodies in the vascular tissue but no obvious virus particles. I attended the lecture by Dr. Doi at the International Plant Pathology Congress in London where he announced the mycoplasma (now termed phytoplasma) infection of plants. Rushing back, we had another look at the electronmicrographs and realized what the causal agent of Sandal spike was (9). This discovery prompted some further work on plant mycoplasmas with Bob Horne who was head of Ultrastructure Studies Department at JI. It also led to a visit to India, with an interesting scene at London's Heathrow Airport explaining to a large number of customs officers about the plant material (with an import license) that I had in my carry-on case.

Over the next few years I made fundamental studies on a range of viruses including *Cucumber mosaic virus*, *Pea enation mosaic virus*, *Broad bean mottle virus*, *Broad bean wilt virus*, *Sugar beet yellows virus*, and the first virus to be described in ferns using the available technology. Techniques such as protoplasts, in vitro translation systems, and acrylamide gel electrophoresis (in tubes) were developed and were adopted widely in my research. In working with such a range of viruses, I became interested in taxonomy and was in contact with the International Committee on Taxonomy of Viruses (ICTV). Working with Moshe Bar-Joseph, we proposed the Closterovirus group (based on the Greek klosteros, a fine thread, to describe the virus particles). The ICTV met to discuss the Closterovirus proposal at an international meeting, and one of the committee came out to find me. He said, "We are worried about the name as Kloster means a monastery in German." "Don't worry," I replied, "they are all plus-strand." This proposal was then accepted.

SABBATICAL YEAR IN DAVIS

In the early 1970s I had several approaches to spend a sabbatical year in the United States. Tucson, Arizona with Milt Zaitlin looked very

***Alfalfa mosaic virus* (AMV):** type species and only member of the *Alfamovirus* genus of the *Bromoviridae* family. Has a broad host range causing significant disease in some crops; transmitted by aphids in the nonpersistent manner. The ssRNA genome is multicomponent, packaged in three sizes of bacilliform particles

attractive, but then Milt moved to Cornell. At that time I had an offer from Bob Shepherd in UC Davis to work on the then-enigmatic only DNA virus in plants, *Cauliflower mosaic virus* (CaMV). I accepted this invitation with alacrity as sabbaticals are not only for broadening one's work experience but also for seeing the country and broadening one's overall experience. Davis seemed an ideal center on both counts, not only having good science but also being equidistant from the California coast and the high Sierra Nevada. So in December 1973 we, my wife and five children aged between 2 and 9 years, set off for California and a very rewarding year. My work with CaMV was to further characterize the virus using the then relatively new gel electrophoresis techniques (tube acrylamide gels). The first problem that I found was the very low yield of virus by the purification techniques then available. Once I had worked out how to disrupt the inclusion bodies that contained much of the virus, very steady progress was made with the rest of the characterization. In the middle of 1974 I heard rumors about some strange new enzymes called restriction endonucleases that could be used to characterize DNA by cutting it at specific sites. I took some CaMV DNA to Herb Boyer's lab in San Francisco and was introduced to the new world of EcoRI, SalI, and BamHI (the three enzymes then available), flat-bed agarose gels, and ethidium bromide. We did the first cuts on CaMV DNA, which, in retrospect, were probably the first cuts on any plant-related DNA. My only regret is that I have not kept the Polaroid photograph of the gel.

THE CAULIFLOWER MOSAIC VIRUS YEARS

On return to JI from my sabbatical year, I continued with various research projects that were still ongoing and also started a project on CaMV. I also began to set up the new recombinant DNA technologies, essentially introducing them to the JI. We had to build our own equipment and extract our own enzymes—at least we could then buy agarose and not have to make it from agar. The CaMV work initially focused on the physical structure of the genome and transcription from it using the new gel techniques. I made a collection of CaMV isolates from around the world and used restriction endonuclease mapping to study the variation (5); this was several years before the term RFLP mapping was coined. In the United States, the controversy about the use of recombinant DNA technology resulted in the Asilomar Conference and promulgation of subsequent guidelines/regulations. In January 1978, a joint European-U.S. workshop on "Risks for recombinant DNA experiments involving the genomes of animal, plant and insect viruses" was held in a hotel near London. Roy Markham was invited and asked me to attend in his place. It was an intensive meeting with everything recorded, including conversations at the lunch and dinner tables, and it introduced me to the concept of risk assessment for this technology. We had started to experiment with the possibilities of using CaMV DNA as a vector for genetic engineering in plants, which brought us into contact with the regulators, the Ministry of Agriculture, Food and Fisheries (MAFF), who had responsibility for regulating the manipulation of plant "pests." On application for a license for our work, it soon became apparent that we knew much more about the technology than did MAFF! The contact with biosafety regulation led me to consider the potential risks from use of viral sequences in transgenic plants (6) and subsequently to be involved in the GM release controversy and training of regulators (see below).

We knew that CaMV had a DNA genome and we started work on its replication using *Simian virus 40* (SV40) as a model. We spent a long time getting nowhere as our observations did not even start to fit the model. I was due to give a departmental seminar on this work and so started the previous weekend to prepare. I suddenly realized that retroviruses had a DNA phase in their replication and so kept on dashing from home to the JI library, looking up facts about retroviruses and finding that they applied to CaMV. Suddenly, the light dawned that

***Cauliflower mosaic virus* (CaMV):** type member of the *Caulimovirus* genus of the *Caulimoviridae* family. Transmitted by aphids in the semipersistent manner, requiring a virus-coded helper factor, it can cause some losses in Brassicas. Its dsDNA genome is encapsidated in bacilliform particles and replicates by reverse transcription

Rice tungro virus disease: caused by a complex of two viruses, *Rice tungro bacilliform virus* (RTBV) and *Rice tungro spherical virus* (RTSV). RTBV, the type and only member of the *Tungrovirus* genus of the *Caulimoviridae*, causes moderate symptoms in rice; no natural vector is known. Its dsDNA genome is encapsidated in bacilliform particles and replicates by reverse transcription. RTSV is the type member of the *Waikavirus* genus of the *Sequiviridae* family

CaMV replicated by reverse transcription—the first plant virus known to do this. It was one of those moments that makes academic research really rewarding. The replication model fitted all our observations, especially explaining the unusual transcripts that we had noted. I put this over at the seminar and there followed a three-hour discussion with much input from the graduate student who had been working on the SV40 replication hypothesis. Several other groups were working on this model, and in later discussions we found that we had beaten them to the idea by six weeks. We published in a rapid turnover journal (8) but, in retrospect, should have sent our results to *Nature* or *Science*; however, we had had some bad experiences with those journals, which were going through a phase of apparently not liking plant papers.

RICE AND THE ROCKEFELLER FOUNDATION

In the mid 1980s we had many visits from representatives of companies and organizations interested in the potential for DNA recombinant technology for crop improvement. They would visit the JI and several of us would each give them half an hour or so to talk about our work. At that time most of our funding came from the Government Research Council and there was little outside grant funding. I realized the limitations of being restricted to the core funding and obtained a grant from the first European Union (EU) biotechnology funding initiative (under Framework Program 1). Subsequently, I have had funding from Framework Programs 2 to 5, probably one of the few people to have had a "full house" of such funding. However, most of these visits from company and organization representatives were fruitless, with them saying either, "Very interesting and we will be in touch later," or "Can we have full exclusive access to your technology?" One of the visits was from Gary Toenniessen of the Rockefeller Foundation (RF), which was setting up the Rice Biotechnology Program. After talking with him for some time, he gave the first answer. Unlike all the others, I got a letter a couple of months later asking if I would chair a brainstorming session at the International Rice Research Institute in the Philippines on the potential of this technology for controlling rice viruses. I read up on rice viruses on the flight out, chaired the session, and then reported the outcome to the RF Scientific Advisory Committee. There were parallel sessions on fungal and bacterial diseases of rice chaired by American scientists who were very aware of the possibilities of large grants. The intensity of competition for grants was new to me and a very revealing experience. Some weeks later I had a letter from Gary Toenniessen inviting me to apply for a grant to work on rice tungro virus disease, a complex between a DNA pararetrovirus, *Rice tungro bacilliform virus* (RTBV), and an RNA virus, *Rice tungro spherical virus* (RTSV); neither virus had been characterized molecularly. This started a ten-year contact with the RF and much productive work. There were three features of the RF Rice Biotechnology Program that really impressed me. First, they would give grants for similar work to two or more groups. They also funded Roger Beachy for work on rice tungro viruses and this led to competitive collaboration between the two groups. They had regular meetings of the whole program at various locations in tropical countries (it was remarkable how many accompanying persons there were at the meeting in Bali, Indonesia). From the presentations at these meetings, which were very intense and competitive, the Scientific Advisory Committee played a major role in defining the direction of the program. Third, application for renewal of the grant had to be made in person before the Scientific Advisory Committee, a daunting task. The committee members were very sharp and could see through any attempts at bluffing—I met one senior scientist coming out in tears from his appraisal. For studying rice tungro and its leafhopper vector, we were able to capitalize on the fact that we do not grow rice in the United Kingdom. Using a "third country quarantine" approach, we obtained and compared isolates of the two viruses from a wide range of countries in South and South-East Asia. This involved collecting trips

out to farms and meeting the farmers, which I found very informative and rewarding. One interesting trip was to Burma (Myanmar) where tungro had not previously been recorded. As the plane was coming in to land at Rangoon (Yangong) airport, I was looking out at the rice paddies and saw characteristic yellow patches indicative of tungro. I was hosted by Ministry of Agriculture officers who, when we met, asked, "Where do we go?" I suggested that we follow the flight path of incoming airliners, and we found the first record of the disease in that country. The work on rice tungro was very productive and led to the detailed description of the two causal viruses and a large number of attempts to produce transgenic rice to control the diseases. However, the latter proved very difficult and remains a challenge.

The success with European Union (EU) and RF funding and the reduction in core funding led to a change in atmosphere at JI, and the emphasis moved to the need for grants. The director had asked me earlier to be the international liaison officer, which meant keeping a drawer of files on grant opportunities and encouraging colleagues to apply. The drawer expanded to a whole filing cabinet and the task was taking up more and more of my time. I persuaded the director that it was a full-time job, and so someone else was appointed. The remit then grew from one office to a whole department. One of the grants that I obtained was from the McKnight Foundation Crop Collaborative Research program. I was approached by Frank Richards of Yale University to be the plant virologist on a team from Yale, Fudan University (Shanghai), and JI to work on the use of transgenes expressed in the bacterial symbiont *Wolbachia* to make the rice planthopper incapable of transmitting *Rice stripe virus* (RSV). This sounded intriguing: It was a "green" approach to controlling the virus disease as it did not involve killing the vector. We worked on the molecular biology of the virus, identifying target genes, and making short-chain antibody constructs that could be expressed in *Wolbachia*. The work on characterizing *Wolbachia* and developing transformation systems was done at Yale and subsequently at the University of Queensland, Australia when Scott O'Neill moved from Yale. The Shanghai team studied the epidemiology of RSV and developed containment systems so that any transgenic insects could be field tested. Despite our considerable progress, the transformation of *Wolbachia* proved very difficult and thus far all the elements of the system have not come together. Dealing with the McKnight Foundation was very different from the RF. The emphasis was on collaboration and all the grantees were treated as family—a very interesting contrast in approach.

THE GATSBY FOUNDATION AND BANANAS

In the mid 1990s the Gatsby Charitable Foundation (set up by the Sainsbury supermarket family) made a study on how collaborative links between institutes in the U.K. and those in Africa could best benefit African agriculture. They selected a link between the JI and the International Institute for Tropical Agriculture (IITA) in Ibadan, Nigeria. I was asked to set up the co-ordinated program and we obtained a shopping list from IITA from which we selected 6 projects that were compatible to the research programs of both institutes. We then had a meeting at JI to thrash out details of the collaborative program and divide up the Gatsby Foundation grant—this was the first time that I had a grant before the project application! One project was to develop a diagnostic system for the detection of *Banana streak virus* (BSV) in the IITA breeding material. IITA had developed advanced breeding methods for African bananas but these were bedevilled by the high rate of BSV in some of the elite lines that precluded international distribution. As BSV is a badnavirus, this research fitted very well with my project on the variation of RTBV. We soon started getting very unusual results with hybridization signals from all the plants we tested, be they symptomatic or asymptomatic. It dawned on us that genomic sequences of BSV were integrated into the banana genome, a very unusual situation among

***Rice stripe virus* (RSV):** a member of the *Tenuivirus* genus, transmitted in a circulative propagative manner by planthoppers, and causing significant losses of yield in rice. Its ssRNA genome is divided into four or more components each encapsidated by nucleoprotein to form flexuous particles

International Institute for Tropical Agriculture (IITA): IITA, one of the institutes of the Consultative Group on International Agricultural Research, a nonprofit organization to find solutions for hunger and poverty through research for development activities. See **http://www.iita.org**

***Banana streak virus* (BSV):** member of the *Badnavirus* genus of the *Caulimoviridae* family. Transmitted by mealybugs, it causes moderate to severe disease of banana. Its dsDNA genome is encapsidated in bacilliform particles and replicates by reverse transcription

Cartagena Protocol: The Cartagena Protocol on Biosafety is an international agreement on biosafety, as a supplement to the Convention on Biological Diversity. See **http://www.cbd.int/biosafety**

plant viruses. We became aware that Ben Lockhart and Neil Olszewski at the University of Minnesota were also working on this difficult problem and so we set up a collaboration with them. Using two different approaches, we discovered that, under certain circumstances and in certain varieties, the viral integrant could be activated to give episomal infection, a situation completely new to plant viruses (2, 11). We then had to develop diagnostics to detect both episomal virus and activatable integrants and distinguish between them.

The JI is core funded by a Government Research Council and so the employees are scientific civil servants. In the 1990s civil servants were compulsorily retired at the age of 60. The BSV story was being uncovered as I was reaching this age, whereas I would have liked a further 5 to 10 years working on various factors involved with integrated sequences and their activation. However, as I still had several grants running when I retired, the John Innes Trustees offered me emeritus status to maintain my links with the Centre; this was their first Emeritus Research Fellowship. So I was able to continue the BSV work, but because of various U.K. and E.U. regulations, I could not personally do lab work and I had to have an employee as a "front man." I was approached by people with a project funded by the Department for Overseas Development to investigate the variation of BSV in Uganda to provide base-line data for an epidemiological study. This involved several visits to Uganda to collect material from remote farms in the banana-growing region, which extends from the far west (bordering the Congo) to the Kenya border. It was great to return to that beautiful country but it showed me both the problems they were having with BSV causing losses of up to 50% of their staple crop, as well as the repercussions of the HIV/AIDS epidemic. We brought back many samples to the JIC and a postdoc, Glyn Harper, and colleagues identified 15 different, but related, virus species causing banana streak disease (1).

There was increasing interest in Europe about integrating plant pararetroviruses, and a group of us were successful in a bid to the EU Framework Program 5 to study the biodiversity and role of integrated pararetroviral sequences. The project, called PARADIGM (Pararetroviruses: diseases, integration and genomes), involved labs from Austria, France, Germany, Spain, Switzerland, and the United Kingdom; as I could not run a lab on this grant, I was given an advisory role keeping me in touch with this advancing field.

RETIREMENT

As noted above, I had to retire at the age of 60. Although this was very frustrating research-wise, it opened up some new opportunities. These included giving lecture courses on plant virology in various countries including China—one involved 14 one-and-a-half-hour lectures in 7 days to a group of 30 graduate students in Beijing, a task that makes university lecturers in the U.K. blanch!

One opportunity linked my earlier interests in biosafety of GM organisms with those of agriculture in tropical developing countries. It is widely recognized that the application of GM technology could help to ameliorate some of the constraints to food production in developing countries, especially those with food insecurity. The Asilomar Conference in the United States in 1975 and the Ascot meeting in Europe mentioned above led to an international regulatory structure for GM crops encapsulated in the Cartagena Protocol on Biosafety (2000). Although the Protocol deals with transboundary movement of GM products, it essentially means that signatory countries have to adopt national biosafety regulations. However, there is a great difference between adopting such regulations and implementing them; the implementation requires human capacity with the ability to understand the subject and to make informed decisions. I was approached by George Tzotzos, Chief of the Biodiversity Unit at the United Nations Industrial and Development Organization (UNIDO) in Vienna, Austria to help develop a computer-based decision-assisting system for GM crops. This led to discussion about how to

improve human capacity in this area and to the idea of mounting an e-learning diploma course. We piloted the course for two years at the University of Concepcion, Chile and learned a great deal about how to teach the complexities of the subject, ranging from molecular biology to risk assessment and regulatory structures, to mainly mature students from a wide range of backgrounds. I had the interesting challenge of designing e-lectures on molecular biology for lawyers! This course is now being expanded and covers South America, Africa, and South-East Asia (see **http://binas.unido.org/wiki**).

PLANT PATHOLOGISTS AND DEVELOPING COUNTRIES

When one looks back on one's career, one can see challenges and opportunities for the younger generations. prompting the thought, "If only I was 30–40 years younger I would want to do this or that"!! But this reaction has to be viewed in an environment of decreasing official commitment to plant pathology, and especially virology, in many industrialized countries. These countries have food surpluses, but the reduction in capacity and experience is leaving them exposed to dealing with an unexpected epidemic of a new pathogen. However, this danger pales into insignificance when compared with the potential impact that the application of plant pathology, be it applied field pathology or basic molecular pathology, can pose to the current and especially emerging food security situation in many developing countries.

It has been argued that there is currently enough food to feed the world's population and that the shortages are a matter of distribution. This argument leaves aside a number of questions such as who pays for the distribution, the food preferences of different cultures and the role of the farmers who are the major proportion of the population in developing countries. It also does not take into account the diversion of potential food supplies for bioenergy, the likely effects of climate change, and, most of all, increases in population.

Africa is recognized as the continent where most of the current problems occur. Famines, food shortages, and disasters are frequently in the news. However, given the predictions for population increases between now and 2050, it is obvious that the problem of food security will increase dramatically. **Figure 1** shows the predicted increases in the populations of Sub-Saharan countries between the years 2000 and 2050. The data are from the 2006 revision of the estimates of the Population Division of the Department of Economic and Social Affairs of the United Nations; they are the medium variant level, which takes account of prediction of fertility, mortality, and migration and allows for the effect of HIV/AIDS in the countries where more than 1% of the population is infected. The data paint a worrying picture with the population predicted to quadruple in three countries, more than double in most other countries, and only in Southern Africa to increase less than 1.5 times. In contrast, over the same period the population of the United States is predicted to

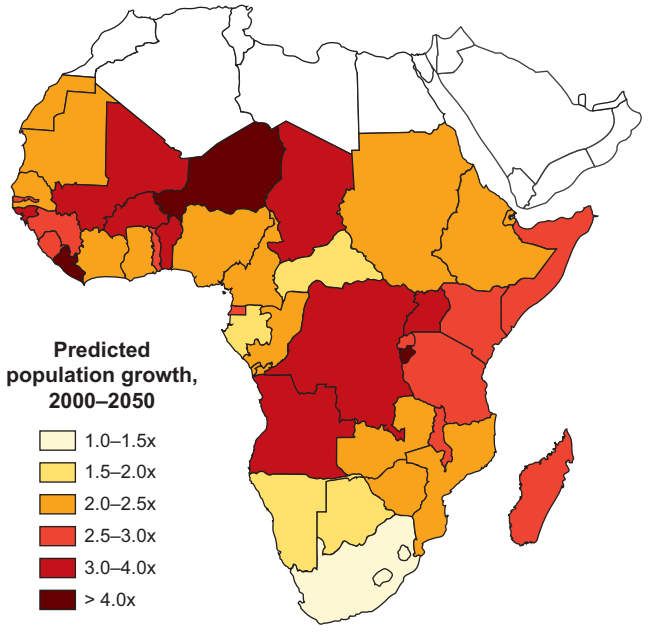

Figure 1

Predicted population changes in Sub-Saharan African countries 2000–2050. (Data from UN Population Division).

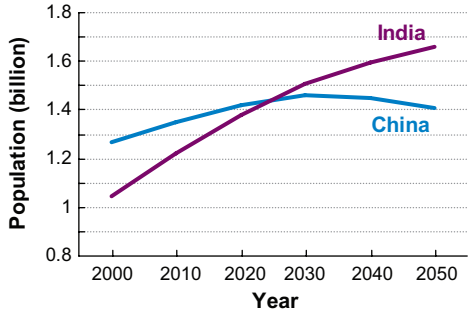

Figure 2

Changes in predicted populations of China and India.

grow by 1.4 times and that of the United Kingdom by less than 1.2 times.

China and India are regarded as being among the more rapidly advancing of the developing countries with expanding economies and rapid industrialization. However, according to the population predictions up to 2050 (**Figure 2**), the population of China peaks at around 2030 and then decreases, whereas that of India overtakes that of China in the mid-2020s and continues to increase. Is this going to cause a repeat of the food famines of the 1950s in India?

In scenarios such as those detailed above for Africa and India, what can plant pathologists do? It is estimated that losses due to pests and diseases reduce the yield of a crop by 25%–30% of its potential. Thus, if these losses could be controlled, yield increases would be far greater than those from most short-term breeding programs. I think that there are three approaches that plant pathologists (and funding agencies) from industrialized countries can take.

First, from my experience, I consider that the most efficient approach to a tropical disease problem is by a cooperative effort between institutions in industrialized countries and those in developing countries. This strategy capitalizes on the strengths of both sets of institutions—the advanced technologies in the industrialized countries and the field expertise in the developing countries. Most attempts to transfer advanced technologies to least developed countries have been unsuccessful mainly owing to problems with infrastructure and human capacity. The focus needs to be on the native tropical crop rather than the introduction of new untried crops that might succumb to new and unknown diseases. The lessons of the introduction of cocoa, cassava, and maize from Central and South America into Africa where they became infected with indigenous viruses (*Cacao swollen shoot virus*, *African cassava mosaic virus*, and *Maize streak virus*, respectively) should not be ignored.

Second, the transgenic approach to disease resistance has features that show more potential for durability than the breeding of many natural resistance genes. The increasing understanding at the molecular level of the interactions between the pathogen and host can lead to targeting of the pathogen at a critical site. The transgenic approach is also more rapid than conventional breeding. However, it is circumscribed by regulations and by adverse public opinion in many industrialized countries, driven in many cases by unbalanced presentation and misrepresentation of scientific fact. Plant pathologists and all biological and molecular scientists should take part in public discussions and present a balanced view of the risks and benefits. Plant pathologists should also place a greater emphasis on crops and pathogens of orphan crops important in developing countries.

Third, the challenges for producing enough food will come not only from population increases but also from factors such as climate change, which will cause major changes in the pest and disease problems worldwide. I feel that scientists from various disciplines should get together to make predictions of how the situation is likely to change, and plant pathologists should direct their research with these different circumstances in mind. Coupled with the new technologies, this collaboration should change plant pathology from being a "fire brigade" exercise dealing with problems after they arise to being proactive and prepared for future eventualities.

DISCLOSURE STATEMENT

The author is not aware of any biases that might be perceived as affecting the objectivity of this review.

LITERATURE CITED

1. Harper G, Hart D, Moult S, Hull R, Geering A, Thomas J. 2005. The diversity of *Banana streak virus* isolates in Uganda. *Arch. Virol.* 150:2407–20
2. Harper G, Osuju JG, Heslop-Harrison JS, Hull R. 1999. Integration of banana streak badnavirus into the *Musa* genome: molecular and cytological evidence. *Virology* 255:207–13
3. Hull R. 1964. Spread of groundnut rosette virus by *Aphis craccivora* (Koch). *Nature* 202:213–14
4. Hull R. 1970. Studies on alfalfa mosaic virus. IV. An unusual strain. *Virology* 42:282–92
5. Hull R. 1980. Structure of the cauliflower mosaic virus genome. III Restriction endonuclease mapping of thirty-three isolates. *Virology* 100:76–90
6. Hull R. 1990. Non-conventional resistance in plants—concepts and risks. *Proc. 19th Stadler Conf.*, ed. GP Gustafson, pp. 289–303. New York: Plenum
7. Hull R, Adams AN. 1968. Groundnut rosette and its assistor virus. *Ann. Appl. Biol.* 62:139–45
8. Hull R, Covey SN. 1983. Does cauliflower mosaic virus replicate by reverse transcription? *Trends Biochem. Sci.* 8:119–21
9. Hull R, Horne RW, Nayar RM. 1969. *Mycoplasma*-like bodies associated with sandal spike disease. *Nature* 224:1121–22
10. Hull R, Plaskitt A. 1970. Electron microscopy on the behaviour of two strains of alfalfa mosaic virus in mixed infections. *Virology* 42:773–76
11. Ndowora T, Dahal G, LaFleur D, Harper G, Hull R, et al. 1999. Evidence that badnavirus infection in *Musa* can originate from integrated pararetroviral sequences. *Virology* 255:214–20