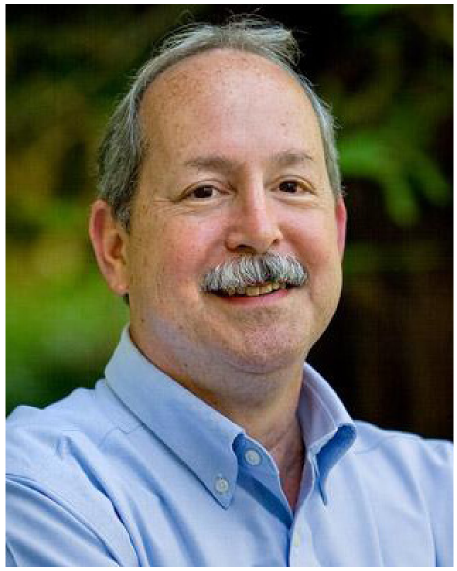
ASPB Pioneer Member

Elliot Meyerowitz

I grew up in the Maryland suburbs of Washington D.C., where I attended the local public schools. After the usual high school science courses, I went to Columbia University as a freshman in 1969, with the idea of majoring in some area of science. An introductory biology course that emphasized quantitative and mathematical approaches in molecular biology, given by the physicist Cyrus Levinthal and the virologist James Darnell, led me to declare a biology major. I worked part time in the Levinthal lab during my junior and senior years, and full time (at Levinthal's summer lab at Woods Hole) in the summers of 1972 and 1973. The project on which I worked, where the shape and branching pattern of fish neurons was analyzed, seems to have set the stage for what I have done afterward, as it introduced me to microscopy, 3D image reconstruction, and the use of computers in biology. As a graduate student at Yale with Douglas Kankel, I studied the development of *Drosophila* eyes and brains and the connections that form between them, by use of genetic mosaics. Just as for my undergraduate work, what I learned - developmental genetics – was highly influential in my lab's later work.

At Yale I was first introduced to plant development and plant genetics. I took no botany courses as an undergraduate, and although I was a student in the animal side of the Yale Biology Department, I had plant physiology lectures



from Art Galston and Mary Helen Goldsmith. I also attended the plant developmental biology journal club in Ian Sussex's lab, with an interest in seeing if plant developmental biology could be developed along genetic lines, as was being done using *Drosophila*. At that time (1975) I was pointed (by my friend and Sussex student, Jim Wong) to a review article on *Arabidopsis* genetics by George Rédei, in Annual Review of Genetics, and an idea was born. When I graduated in 1977 the methods to clone eukaryotic genes were just being developed, and I went to the Stanford Medical School Biochemistry Department as a postdoc in David Hogness's laboratory to learn them, using *Drosophila*.

I became an assistant professor at Caltech in 1980, hired as a *Drosophila* developmental biologist. But I still had an interest in bringing *Drosophila*-style genetics to plant development. With one of my first graduate students, Bob Pruitt, I started growing *Arabidopsis* (the seeds initially came from Bob's uncle, Andris Kleinhofs, a barley geneticist). Bob and I looked at developmental mutants. As a precursor to gene cloning, my first postdoc, Leslie Leutwiler, characterized the size and organization of the *Arabidopsis* genome using reassociation kinetics of genomic DNA. I made an *Arabidopsis* genomic DNA library, and Bob used it to validate Leslie's analysis. Kevin Mossie studied the genome's transposable elements. The plant project engaged the interest of a number of new graduate students and postdocs, leading to the first cloning and sequencing of an *Arabidopsis* gene (Alcohol Dehydrogenase, cloned by graduate student Caren Chang). We also cloned seed storage protein genes (this was done by Patty Pang), and light-harvesting proteins (done by Leslie in collaboration with Elaine Tobin's laboratory at UCLA). In addition, we introduced in situ hybridization to plant research, and produced the first molecularly based genetic map of the *Arabidopsis* genome (an RFLP map for which Caren Chang led the effort); we enlisted the computational expertise of a young Harvard mathematician named Eric Lander, who was later to apply the same methods to the human genome. Some of the developmental mutants we analyzed were homeotic mutations that affected flower development, the most interesting of which were sent to

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us by a Ph.D. student in the van der Veen lab at the University of Wageningen, Maarten Koorneef, who used them in laboratory exercises he developed for undergraduate plant breeding labs. He was soon to be a great pioneer of the genetic analysis of hormone function in *Arabidopsis*. In 1985, Pruitt and I published a paper in Science in which we proposed that plant biologists should concentrate on *Arabidopsis thaliana* as a model system that is well-adapted for laboratory use and gene cloning. We soon found there were others, including David Meinke, Chris Somerville, as well as Koornneef, with similar thoughts, and a community began that is still very lively (and much larger) today. As a side note, I mention the influence of the ASPB, as our first flower development paper was published in volume 1, issue 1 of the The Plant Cell in January 1989.

The work on flower mutants, involving many in the lab, especially at the start David Smyth, a visiting professor from Australia and John Bowman, a graduate student, led to models for genetic interactions that act in organ specification (the ABC model). Molecular analysis of the homeotic mutants that John and David characterized, and additional mutants characterized afterward, launched the careers of Marty Yanofsky, Hong Ma, Usha Vijayraghavan, Gary Drews, Detlef Weigel, Koji Goto, Tom Jack, Leslie Sieburth, Zhongchi Liu, Joshua Levin, Beth Krizek, Hajime Sakai, José Luis Riechmann, Robert Sablowski, Xuemei Chen, Doris Wagner, Eva Ziegelhoffer, Marcio Alves Ferreira, Chiou-Fen Chuang, Jeff Long, Hao Yu, Yuanxiang (Ansel) Zhao, Annick Dubois, Pradeep Das, Toshiro Ito, Catherine Baker, Patrick Sieber, Frank Wellmer, Carolyn Ohno, Yuling Jiao, Adrienne Roeder, Xiaolan Zhang, Nat Prunet and others who are now familiar as international leaders in plant developmental biology. Some epigenetically inherited flower phenotypes figured out by Steve Jacobsen, and involvement of homologues of *Drosophila* epigenetic regulators pioneered by Justin Goodrich, were among the opening moves in the now-large area of plant epigenetics. Another venture was to understand floral organ number, which led to the CLAVATA system and plant peptide hormones. Steve Clark, Bobby Williams, and Jenn Fletcher, along with others (including a productive collaboration with Rüdiger Simon), played a central role in starting this line of research, which continued with the work of Venu Reddy, Zach Nimchuk and Yun Zhou, with additional work in my lab and the labs of many others.

Not all the work was on flowers and meristems - our lab was the first to clone a plant hormone receptor, that for ethylene, which was done by Caren Chang when she returned to my lab as a postdoc. She did this work with another postdoc, Tony Bleecker, who as a graduate student with Hans Kende had isolated the first ethylene receptor mutations. Cloning of the receptor was followed by experiments that led to an understanding of the receptor gene family and the negative function of the receptor, much of it done by graduate student Jian Hua.

To really understand developmental phenotypes, we started using laser scanning confocal microscopes to get quantitative real-time three-dimensional images of growing plants at subcellular resolution. This effort was led at its start by Mark Running, then joined by Venu Reddy and Marcus Heisler, and continued into realms of plant regeneration and graft formation in work done by Sean Gordon, Kaoru Sugimoto and Charles Melnyk. In Marcus's hands, and in collaboration with Jan Traas, Arezki Boudaoud and Olivier Hamant in France, as well as then-Jet Propulsion Lab (and now University of California Irvine) physicist Eric Mjolsness, and then-Caltech postdoc, presently Director of the Sainsbury Laboratory at Cambridge University, physicist Henrik Jönsson, this led to computational models of meristem growth and phyllotaxis, studies of auxin action in meristems (starting with Marcus's work and later including the work of Wuxing Li, Cory Tobin and Yuling Jiao), and the recognition that the morphogenetic fields that control cell type and organ shape can be physical as well as chemical. Mechanical control of development was an area started in my laboratory by postdoc Liz Haswell, whose cloning of

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stretch-activated channels opened this new area. The relationship of mechanics and development is still a frontier area in biology (pioneered by Paul Green, who visited our lab a number of times in the 1980s to discuss flower development, but not biomechanics), and is very much a continuing research area in my lab and that of our collaborators.

I don't want to give the impression that our *Drosophila* work ended when the plant work began – my lab continued to work on flies and their nervous system until the early 1990s, with a group of students and postdocs who have gone on to great success in animal developmental biology; an example of one of our results (from work of Alex van der Bliek) was the first cloning of a dynamin gene, and the demonstration (in collaboration with Sandy Schmid's lab) that dynamin acts in late stages of endocytosis. But as the plant work ramped up, the fly work ramped down and finally stopped – plants were just too much fun, and the growing community of *Arabidopsis* labs too lively and collegial not to devote a full effort.

In 2011 and 2012 I took a two-year leave from Caltech in which I served as the Inaugural Director of the newly established Sainsbury Laboratory at the University of Cambridge (SLCU) in the United Kingdom. Starting there and afterward I have had a collaborative research program working on mechanical control of development with scientists that included an impressive group of postdocs, starting with Ray Wightman and Arun Sampathkumar (Arun was first at SLCU and then at Caltech), and later Pauline Durand-Smet (who first was at Caltech and then SLCU) and Charles Melnyk, Christoph Schuster, Benoit Landrein, Yi Zhang, Pau Formosa-Jordan, Hayk-George Drost and Weibing Yang. Some of the work at SLCU followed from studies of the developmental roles of cytokinin hormones that were done at Caltech by Sean Gordon, Vijay Chickarmane, Ying Wang and Paul Tarr. At SLCU, Benoit Landrein showed that cytokinin precursors are a signal from roots to shoots of nutrient status that controls meristem size and flower number; Weibing Yang followed this by showing the mechanism by which cytokinins cause increased cell division in the shoot meristem by cytokinin-regulated nuclear accumulation of a transcription factor that initiates cell division.

When Brian Larkins telephoned to tell me that my former lab members had made me a Pioneer of the ASPB, he invited me to write this autobiography, keeping in

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Many of the lab alumni are in this photo of our 2011 lab reunion (photo credit José Luis Riechmann).

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mind that the audience should be the students who will be the next generation of plant scientists. This implies that I ought to give some advice. Implicit in the narrative above is one piece of advice, that you should do what you think is interesting and fun, and not worry too much about a career or where you might fit into a profession – following your interests seems to me to be the path to professional success. Another clear lesson is that the greatest assets a lab can have are the students, postdocs, and visiting faculty (who in my lab have included not only David Smyth, but also Michael Frohlich, Ann Hirsch, Prakash Kumar, Nelu Negrutiu, Kathrin Schrick, Ottoline Leyser, Toshi Takai, Ivo Grosse, and others, who have made major contributions not only to our work, but also to the education of the others in the lab, including me). Your job, once you are a lab head, is to make sure the members of your lab can work unimpeded, are encouraged to stay engaged and productive, and can take their projects with them to establish their own laboratories when they leave.

We have done what I think is exciting and pioneering work, some of it is even in textbooks. I don't know that any of it will be that important or even remembered 50 or 100 years from now – if science goes as it should, it will be forgotten and replaced by new discoveries and new ways of thinking. The real success of the lab has been the success of its students and postdocs. This is our lasting contribution, unlike the papers, because former lab members and their students, and students' students, will make the new discoveries that will make our current work and ideas obsolete, leading science ever forward.

To see who some of the lab members have been, and who they have trained, take a look at our academic family tree: **https://academictree.org/plantbio/tree.php?pid=13709**

And finally, the work continues—I haven't mentioned most of the current members of my laboratory, but you will be hearing from them!