A Brief History of *Schizosaccharomyces pombe* Research: A Perspective Over the Past 70 Years

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ABSTRACT Since its humble start as a model organism in two European laboratories in the 1940s and 1950s, the fission yeast *Schizosaccharomyces pombe* has grown to become one of the best-studied eukaryotes today. This article outlines the way in which interest in *S. pombe* developed and spread from Europe to Japan, North America, and elsewhere from its beginnings up to the first International Meeting devoted to this yeast in 1999. We describe the expansion of *S. pombe* research during this period with an emphasis on many of the individual researchers involved and their interactions that resulted in the development of today's vibrant community.

THE history of molecular and genetic research using the fission yeast *Schizosaccharomyces pombe* dates back to 1946 when Urs Leupold (see Figure 1 for photographs of some of the people involved in the popularization of *S. pombe* as a model organism) was given his first strain to analyze. Until the mid-1980s, however, this yeast was regarded by most researchers as a minor organism with a far lower profile than its distant cousin, the budding yeast *Saccharomyces cerevisiae*. At "yeast" meetings, *S. pombe* research was viewed as something of a curiosity. Since that time, research on *S. pombe* has expanded to the point where it is one of the best-characterized model eukaryotes for studying cell biology at the molecular level. This can be seen by the rise in the number of publications on *S. pombe* from ~50 in 1985 to almost nine times that number in 1999 (Hoffman *et al.* 2015), the year of the First International Fission Yeast Meeting held in Edinburgh (Partridge and Allshire 2000). Much of the interest in *S. pombe* came in response to the cell-cycle studies carried out in the 1970s and 1980s that were later recognized with a 2001 Nobel Prize in Physiology or Medicine to Paul Nurse (Figure 1). In addition, growth in the fission yeast community led to *S. pombe* becoming the sixth eukaryote to have its entire genome sequenced at a time when genomic sequencing was still a major undertaking (Wood *et al.* 2002).

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The aim of this article is to take a brief backward look at the early history of *S. pombe* research, with particular interest in how research using this yeast spread from two European laboratories in the 1950s to its establishment as a major model organism studied by >300 laboratories around the world today. Research on *S. pombe* has been well documented and summarized in two books (Nasim *et al.* 1989; Egel 2004) as well as in review articles (Russell and Nurse 1986; Hoffman *et al.* 2015). This article presents the story of the growth and development of the *S. pombe* community from its beginnings to the maturity of the research field at the time of the First International Fission Yeast Meeting held in 1999. We hope that this will be of interest to new and established *S. pombe* researchers and to people working on other organisms but who share an interest in how today's *S. pombe* community came into being. Several of the central figures included in this Perspectives have written of their own entries into *S. pombe* research including Urs Leupold (Leupold 1993), Murdoch Mitchison (Mitchison 1990), Richard Egel (Egel 2000), Paul Nurse (Nurse 2002), and Mitsuhiro Yanagida (Yanagida 1999) (Figure 1). This Perspectives article seeks to merge these stories into a single narrative and describe the key roles that several other people have played in building the *S. pombe* community.

S. pombe has nearly always been an organism where research has been driven purely out of curiosity and academic interest, while *S. cerevisiae* has been of practical use for millennia before the modern era for bread-making and brewing. Because of this, the physiology and metabolism of *S. cerevisiae* have long been the focus of research with a drive toward increasing growth rate or CO2 or alcohol production.

Figure 1 Some of the people responsible for the spread of *S. pombe* research who are pictured in alphabetical order from left to right. (Top row) David Beach (1954), Richard Egel (1941), Peter Fantes (1948), Jerry Hyams (1947). (Second row) Jürg Kohli (1945), Urs Leupold (1923–2006), Maureen McLeod (1949), J. Murdoch Mitchison (1922–2011). (Third row) Olaf Nielsen (1959), Paul Nurse (1949), Paul Russell (1956), Chikashi Shimoda (1942). (Fourth row) Carl Singer (1945–2013), Masayuki Yamamoto (1947), Mitsuhiro Yanagida (1941), Paul Young (1947).

Investigations into the regulation of its metabolism at the levels of enzymes and pathways led to studies of how the cognate genes were expressed, once technology allowed this. Much of the inspiration for these studies derived from studies on bacteria—*Escherichia coli* in particular—and there was a strong focus on molecular biology and transmission genetics, with seminal discoveries by scientists such as Carl Lindegren, Herschel Roman, and Donald Hawthorne, to name but three (Hall and Linder 1993). Work from these laboratories not only established *S. cerevisiae* as a premier genetic model organism, but also created a strong foothold for *S. cerevisiae* research in North America.

In contrast, *S. pombe* was initially studied because of interest in its cell biology. Research started in the 1940s and early 1950s in two main areas: the mating-type system, which led to investigation of the sexual cycle, and the growth and division processes that comprise the cell division cycle.

Europe and the First Pioneers

The Swiss scientist Urs Leupold is considered the father of *S. pombe* genetics. In 1946, during a visit to the Carlsberg Laboratory in Copenhagen at age 23, he was introduced to the yeast by Øjvind Winge, who recommended that Leupold study its homothallism for his Ph.D. studies (Leupold 1993). (Today it is unclear what specifically motivated Winge's suggestion.) While the *S. pombe* strain that Leupold received from Winge turned out to be largely infertile, he later received a Swiss isolate from a strain collection in Delft in The Netherlands. From this sample, he identified two distinct

homothallic strains (mating types h^{90} and h^{40}), two heterothallic strains (mating types h^+ and h^-), and one sterile strain (Leupold 1949). Three of these strains, 968 h^{90}, 972 h^-, and 975 h^+, have been the founders for nearly all subsequent genetic studies on *S. pombe*. Being isogenic or nearly so, the widespread use of these strains has enhanced the consistency in data obtained from different labs studying the same set of genes or biological process. Leupold showed that a strain's mating type is controlled by a single genetic locus, now known to be the complex *mat* region containing both silent and expressed genes. During Leupold's career, he and his collaborators made *S. pombe* into a genetically tractable model organism by isolating mutants affected in a variety of processes and constructing the first chromosome maps by classical genetic crosses. He had particular interests in nonsense suppression and recombination, using the multiple copies of transfer RNA genes to investigate ectopic recombination between the dispersed copies. His laboratories, first at the University of Zürich and then at the University of Bern, where he was head of the Institute of General Microbiology, served as the major centers for *S. pombe* genetics for several decades. It seems fitting that after his retirement he returned to studying the sexual cycle of *S. pombe* in a laboratory that he built in his home. One of his final publications (Leupold *et al.* 1991) was a major step leading to the identification of mating pheromones.

It may be easy for today's scientists to underestimate Leupold's impact on *S. pombe* research as measured by literature search results in PubMed and similar databases. There are three reasons for this. First, some of the studies by Leupold were published as proceedings of conferences that were not indexed as publications at the time and therefore are not accounted for in PubMed without subsequently appearing as independent publications in scientific journals. Second, many of the scientists who trained with Leupold spoke and wrote in German and did not publish their work in international English language journals. Finally, as described by his former Ph.D. student Jürg Kohli (Figure 1) "The members of Leupold's group enjoyed almost unlimited freedom for their approaches to research with fission yeast. While he readily provided suggestions and advice for research targets, he also fully supported independent initiatives of his students and visitors" (personal communication). This meant that many of the studies for which Leupold made substantial intellectual contributions did not include him as an author.

At around the same time, in the 1950s and 1960s, Murdoch Mitchison, at the University of Edinburgh, was interested in the pattern of cellular growth between cell divisions. He tried a number of organisms from bacteria to sea urchin eggs before settling on *S. pombe*. Its growth by linear extension and medial division allowed him to obtain a good estimate of the age of an individual cell by measuring its length (reviewed in Mitchison 1990). His primary interest was in the precise patterns of increase between divisions of cellular properties such as total mass or protein content and the rates of overall protein synthesis and of individual proteins and other macromolecules. One line of thought Mitchison had explored in the late 1960s was that cell division was triggered by the accumulation of a molecule (probably a protein) to a critical threshold. By identifying proteins or molecules whose abundance increased during the cell cycle, he hoped to gain insight into the control of division (Mitchison 1971). This hypothesis proved to be correct as shown by the discovery of the mitotic cyclins some 20 years later, although this was done by methods that were distinct from Mitchison's.

In addition to conducting his own research, with the skilled technical expertise of his long-term collaborator Jim Creanor, Mitchison presided over a relaxed and lively lab. They had developed basic and essential techniques for studying the *S. pombe* cell cycle such as how to synchronize cells, visualize the nuclei by staining, and measure the DNA content of culture samples. All these were essential baseline methods for what followed. Paul Nurse arrived in early 1974 and was followed by Kim Nasmyth and one of us (P.A.F.) later that year. Pierre Thuriaux and Michele Minet joined the lab for a year in 1975. These people formed the group who introduced genetic approaches into a lab whose previous investigations into the *S. pombe* cell cycle had been through biochemical and cell physiological methods. Mitchison welcomed the new ideas and spent much of his research time discussing them with his group. He was a generous lab head, not wanting his name to appear as an author on papers from his lab unless he had himself carried out experimental work (Mitchison and Nurse 1985). For this reason, as with Leupold, it is not always easy to identify articles from Mitchison's lab; literature searches are further complicated by his first initial being "J." rather than "M." (for Murdoch, the name by which he was universally known). Mitchison generously hosted a number of guests in his lab [including Paul Young (Figure 1); see below] and again did not always put his name on their publications.

For two decades, much of the research in *S. pombe* was dominated by the laboratories headed by Leupold and Mitchison and later by their former students and postdoc trainees who were now heading their own labs. In addition, other European researchers such as Herbert Gutz, Henri Heslot, Rolland Megnet, and Nicola Loprieno provided additional knowledge about *S. pombe* and generated critical new strains that were key to the development of *S. pombe* genetic research (Gutz *et al.* 1974).

A third European center for *S. pombe* research was established in Copenhagen, Denmark, in the late 1970s by Richard Egel. Egel began his research on *S. pombe* as an undergraduate and later as a Ph.D. student in the 1960s with Carsten Bresch by isolating and characterizing mutants unable to undergo meiosis (Bresch *et al.* 1968; Egel 1973). This represented the first use of a genetic approach to study basic aspects of the *S. pombe* life cycle. The project started when Bresch and Egel were working in Texas at the same time as Gutz, following his visit to Leupold's lab in Zürich. Egel took this system from Freiburg, Germany, to Copenhagen, where his laboratory studied the physiology and genetics of entry into meiosis and was later involved in many related studies.

Along with his own research, Egel played a significant role in the advancement of *S. pombe* research through the sharing of mutant strains and through his many collaborative interactions either as the host to visiting scholars or as a visitor to other fission yeast laboratories (Egel 2000).

While technically not a "First Pioneer," having entered the world of *S. pombe* research as a postdoc with Murdoch Mitchison, no one has had a greater impact on the success of *S. pombe* as a research organism than Paul Nurse. Inspired by Lee Hartwell's pioneering mutant screens for *S. cerevisiae* cell-cycle genes in the early 1970s, Nurse sought to conduct similar studies in *S. pombe*. He therefore visited Leupold's group in Bern for several months, where he learned genetic methods under the guidance of Leupold, Thuriaux, and Peter Munz. Nurse realized, from Mitchison's work, that cell length was intimately related to cell age, and furthermore that blocking the cell cycle with chemical or physical agents led to elongated cells. This led him to look for temperature-sensitive mutants that are defective in cell-cycle progress as seen by their elongation when grown at high temperature. The first such mutants (*cdc*, cell division cycle) were isolated during his time in Bern. He then moved to Mitchison's group to pursue their analysis and isolate additional cell-cycle defective strains. In the mid-1970s a series of articles describing cell-cycle mutants and their use in investigating how the cell cycle is controlled were published by Nurse and colleagues (reviewed in Fantes 1989). This ground-breaking work led them to discover the central role of the Cdc2 protein kinase in the *S. pombe* cell cycle and later to demonstrate the universal role of the protein in regulating mitosis (Nurse 1990, 2002). As part of this work, in collaboration with David Beach (Figure 1), when they were both at the University of Sussex, Nurse developed a procedure for the transformation of *S. pombe*. This allowed researchers around the world to clone the genes for which they had mutant strains (Beach and Nurse 1981). Finally, Nurse has played a central role in promoting *S. pombe* research over the following decades.

S. pombe in Japan

During the late 1970s, three *S. pombe* research groups were set up in Japan. The first of these was that of Chikashi Shimoda (Figure 1), who, after a brief dalliance with *S. cerevisiae*, decided to use *S. pombe* to study the biology of ascospores and spore germination, isolating mutants defective in that process. There were no other *S. pombe* geneticists or molecular biologists in Japan at the time, so Shimoda spent a year in Gutz's lab in Braunschweig to learn *S. pombe* genetic methods and returned to Osaka armed with a collection of strains. He decided to investigate the formation of ascospores, which follows the second meiotic division. Most of Egel's mutants were unable to complete meiosis and failed to produce spores. Egel sent the mutants to Shimoda, whose lab cloned several of the *mei* and related genes required for ascospore formation (Shimoda *et al.* 1985, 1987).

Shimoda's lab in Osaka was also instrumental in providing strains and training for other Japanese *S. pombe* researchers. This included people from the research groups of Masayuki Yamamoto (Figure 1) and Mitsuhiro Yanagida, the two other early Japanese *S. pombe* pioneers, who were setting up their own laboratories at the time. Yamamoto had worked in the United States on bacterial ribosome genes and was looking for a genetically tractable eukaryote to study. He decided on *S. pombe* as it would be a good complementary system to the more intensively studied *S. cerevisiae*. On returning to Tokyo to set up his own lab in 1978, he acquired *S. pombe* strains from Shimoda. His interest in the mechanisms of cell division led him first to investigate the microtubule system, using the genetic approach of selecting for mutants resistant to microtubule inhibitors (Yamamoto 1980). He joined Yanagida's group in Kyoto in 1979 as a junior faculty member and introduced them to *S. pombe* before returning to Tokyo in 1982. His research there was mostly concerned with regulation of the sexual cycle and the switch between mitotic and sexual cycles.

Yanagida had previously worked on bacteriophage morphogenesis with Kellenberger at the University of Geneva and was interested in chromosomal and higher-order DNA structure, as described, along with his entry into *S. pombe* research, in Yanagida (1999). His encounter with *S. pombe* through Yamamoto convinced him that *S. pombe* was an organism the chromosomes of which were worthy of study, and his laboratory went on to isolate and study mutants, including cold-sensitive mutants that showed altered nuclear chromatin morphology (Toda *et al.* 1981). Yanagida's approach was from a more molecular perspective than that of Shimoda and Yamamoto (and many other *S. pombe* scientists at the time) who took a more holistic "whole organism" approach. Fortunately, the "bottom up" and "top down" approaches turned out to complement one another well. Pioneering work from the Yanagida lab on chromosome dynamics, including kinetochore structure and function, has been followed by several other labs investigating telomere structure and function and related areas such as heterochromatin structure, formation, and maintenance (see the *Notable Advances from Fission Yeast Research* section of Hoffman *et al.* 2015). Thus *S. pombe* was firmly established as a research organism in Japan by the early 1980s, and the number of Japanese fission yeast laboratories grew dramatically with 25 groups represented at the First International Fission Yeast Meeting in 1999.

Establishment of a Europe–Japan Community

S. pombe research links between Europe and Japan were strengthened by several factors, including collaborations, increased migration of postdoctoral scientists between the regions, and the establishment of a conference series specifically developed to enhance interactions in the cell-cycle field between labs in Japan and the United Kingdom. As mentioned above, Richard Egel had shared many mutant strains with Chikashi Shimoda, leading to the cloning of

genes involved in meiosis and spore formation. Meanwhile, Iain Hagan, who had carried out his Ph.D. work with Jerry (Jeremy) Hyams (Figure 1) at University College London and then worked briefly with Nurse, went to Japan in the late 1980s to carry out postdoctoral work with Yanagida; and at about the same time, David Hughes, from Peter Fantes's (Figure 1) lab, took up a postdoctoral position with Masayuki Yamamoto. All these interactions helped to lay the groundwork for a series of conferences that solidified the ties between fission yeast labs in Europe and Japan.

Jerry Hyams, noted for having developed biochemical and immunofluorescence methods for *S. pombe* cells in the 1980s (Marks *et al.* 1986), played a central role in strengthening ties between Japanese and British labs through jointly held conferences. As a coordinator for the Society for General Microbiology, he arranged a meeting on *S. pombe* in Warwick in 1990. He contacted the Royal Society for travel funding for overseas speakers and was given a negative response until the name of Mitsuhiro Yanagida was mentioned. At this point, money flowed freely from the British Council, the Royal Society, and its sister organization in Japan, the Japan Society for the Promotion of Science, supporting the workshop and allowing Jerry to travel to Japan to organize it. The workshop was attended by members of most of the major *S. pombe* labs in the world at the time, and some 20 talks were presented over 2 days.

In addition to the 1990 Warwick Meeting, the British Council provided financial support for the establishment of a UK–Japan Cell Cycle Workshop series. This began in 1992 and was organized by Yanagida and Hyams, with additional funding from the Kato Memorial Foundation. Although having a wider focus than just *S. pombe* research, a substantial proportion of those attending were *S. pombe* researchers with a cell-cycle interest. This pattern continued through fairly regular meetings every 2–3 years and continued to strengthen links between the two countries.

North America Enters the Picture

In contrast, researchers in North America and the United States in particular were relatively slow to take up *S. pombe* as a model research organism. There are several reasons for this: during the 1970s and early 1980s the organism had been mostly studied in Europe. In the United States, *S. cerevisiae* had been the subject of intense research and there was great momentum to pursue analysis of its biology. Many of the principal researchers had backgrounds in bacterial and bacteriophage genetics, taking a molecular biological approach. This led to rapid development of the technology needed for molecular genetic manipulations in *S. cerevisiae*. In contrast, rather few molecular studies had been carried out in *S. pombe*, the emphasis having been on its cell biology. Consequently the prospect of starting a project using *S. pombe* seemed less likely to provide a good return on the time invested.

S. pombe research was not completely absent from the New World, however. Anwar Nasim, who had worked within a mutagenesis group at Edinburgh in the early 1960s, returned to the Chalk River Nuclear Laboratories in Ontario to carry out genetic screens to isolate radiation-sensitive mutants (Nasim and Smith 1975). These *rad* mutants were to prove invaluable tools in later investigations into DNA checkpoint function (al-Khodairy and Carr 1992). In addition, two other Canadians carried out important research on *S. pombe* during the 1960s and 1970s. Byron Johnson, working in Ottawa, studied cell morphogenesis, septum formation, and cell division (Johnson and McDonald 1983). Around the same time, Carl Robinow at the University of Western Ontario developed cytological methods for *S. pombe*, including electron microscopy and the first visualization of *S. pombe* chromosomes using transmission light microscopy (McCully and Robinow 1971; Robinow 1977): the use of fluorescent probes such as DAPI had not yet arrived. The studies by Nasim, Johnson, and Robinow were important as they provided a basis for studying mutants with defects in cell growth and cell-cycle processes, but failed to establish a real foothold for *S. pombe* research in North America.

Paul Young, based in Kingston, Ontario, spent a year's sabbatical in 1980–1981 in the Mitchison group to learn *S. pombe* genetics. He collaborated with Fantes in isolating *cdr* mutants that do not show the usual reduction of cell length during nitrogen starvation (Young and Fantes 1987). He returned to Kingston to pursue *S. pombe* research full time. He was also instrumental in the development of a fission yeast course taught at Cold Spring Harbor and of a pair of fission yeast workshops given at Genetics Society of America (GSA) Yeast Genetics and Molecular Biology Meetings as described below. Finally, Young, together with Nasim and Johnson, edited the book *Molecular Biology of the Fission Yeast* (Nasim *et al.* 1989), which served as an important resource for the *S. pombe* community. This was followed up in 2004 by the equally valuable book *The Molecular Biology of Schizosaccharomyces pombe*, edited by Egel (Egel 2004).

In 1981 David Beach, who had collaborated with Paul Nurse in England on the *S. pombe* cell cycle and the mating-type locus (Beach *et al.* 1982a,b), moved to Amar Klar's lab at the Cold Spring Harbor Laboratory. Klar had previously worked on *S. cerevisiae* mating-type switching and was encouraged to carry out similar work in *S. pombe* by Egel. Beach and Klar worked out the details of the mating-type sequences and switching mechanism (Beach and Klar 1984; Egel *et al.* 1984). Beach was subsequently appointed to a group leader position at Cold Spring Harbor and thereafter worked mainly on cell-cycle control.

At about the same time, Paul Russell (Figure 1), as a Ph.D. student in Ben Hall's lab at the University of Washington, started to work on *S. pombe* promoter structure and function (Russell 1983). Russell determined the structure of the cytochrome c gene, the first *S. pombe* gene to be sequenced (Russell and Hall 1982). He showed that the spacing between TATA boxes and transcriptional start sites in *S. pombe* genes showed greater similarity to that of mammalian genes than to *S. cerevisiae* genes (Russell 1983; Russell and Nurse

1986). Russell's switch to *S. pombe* was supported by the presence in the lab of Nasmyth, who had recently completed his Ph.D. with Mitchison in Edinburgh. Russell subsequently joined Nurse's lab as a postdoc to carry out cell-cycle research before returning to the United States to set up his own group at the Scripps Research Institute. His lab studies DNA replication/DNA damage checkpoints as well as stress responses and has been responsible for training many scientists who are running *S. pombe* labs around the world today.

The next wave of *S. pombe* research in the United States took place in the mid- to late 1980s. Gerry Smith, whose background was in bacteriophage lambda recombination, was drawn to *S. pombe* because of the discovery of a meiotic recombination hotspot generated by a mutation within the *ade6* gene that was originally identified by Gutz (Gutz 1971; Ponticelli *et al.* 1988). His lab went on to investigate recombination further by isolating recombination-defective mutants and further hotspots. In addition, Principal Investigators who studied a variety of biological processes in *S. cerevisiae* realized that *S. pombe* might be worth working on, partly because of its increased profile at conferences (particularly yeast and cell-cycle meetings) and in publications. The finding that many *S. pombe* genes contained introns (Russell and Nurse 1986), in contrast to *S. cerevisiae* genes, stimulated interest. This was strengthened by the observation that a mammalian intron is correctly processed in *S. pombe* (Kaufer *et al.* 1985), although later studies showed that this gene, encoding SV40 small antigen, is unusual in this respect (Russell 1989). In addition, while *S. cerevisiae* centromeres could be defined by a 125-bp functional core, *S. pombe* centromeres were >50 kbp in size and resembled mammalian centromeres with respect to their structure (Clarke *et al.* 1986). Meanwhile, the *S. cerevisiae* world was becoming quite crowded and some researchers felt that a sideways move into *S. pombe* might be advantageous. It was also realized that *S. pombe* could be handled at a technical level in much the same way as *S. cerevisiae* on account of its fungal nature and single-cell lifestyle. At the same time, the large phylogenetic distance between the yeasts meant that studying *S. pombe* was likely to lead to insights about genuinely different ways of carrying out the same or similar functions. On the other hand, any systems shared by the two yeasts might be expected to be more widely conserved (Hoffman *et al.* 2015).

Several groups initiated *S. pombe* projects on topics closely related to their *S. cerevisiae* interests. Thus Henry Levin began work on *S. pombe* transposons in Jef Boeke's laboratory (Levin and Boeke 1992), which had expertise in *S. cerevisiae* transposons. Boeke had actually dabbled with *S. pombe* as a postdoc with Gerry Fink 10 years earlier, although nothing other than a sustained interest in this yeast came of it. One author of this perspective (C.S.H.) initiated investigations into the regulation of gene expression at the transcriptional level in *S. pombe* in Fred Winston's lab (Hoffman and Winston 1991), which was studying transcription in *S. cerevisiae*. Winston's interest was in developing an *in vitro* transcription assay and had been encouraged to consider *S. pombe* during a visit to London where he met with Nurse.

The final wave of creation of *S. pombe* labs in the United States was largely achieved by researchers who had worked on the yeast as postdocs outside the country and then returned to set up their own groups. The Nurse lab in particular was instrumental in offering opportunities for postdocs—from the United States and elsewhere—to work on *S. pombe* and become acquainted with handling it. These young *S. pombe* researchers accelerated the growth of fission yeast research by training their own students and postdocs, some of whom went on to establish their own laboratories.

Workshops, Courses, and Conferences

By the mid-1980s, the *S. pombe* community had grown significantly, but was still dwarfed by the size of the budding yeast community and was not yet ready to sustain its own organism-based conference. Between 1983 and 1999, a series of meetings, workshops, and courses helped to increase the number of people working on *S. pombe* and to strengthen the interactions among *S. pombe* labs to a point where the First International Fission Yeast Meeting could be held in Edinburgh in September 1999.

Prior to the 1999 Edinburgh conference, most *S. pombe* research was presented at either topic-specific meetings (such as the UK–Japan Cell Cycle Workshops described above) or at "yeast meetings." There have been three major series of yeast meetings, all held biennially. This includes the Genetics Society of America's Yeast Genetics and Molecular Biology Meeting, the Cold Spring Harbor Laboratory's Yeast Cell Biology (until 1985, Yeast Molecular Biology) meeting, and the International Conference on Yeast Genetics and Molecular Biology (note that the precise names of these meetings have varied over the years). Consistent, however, with the relative size of the two research communities, *S. pombe* talks and posters rarely exceeded 5% of the content of these meetings. This left many researchers to question whether it was worth their time to attend such meetings, creating a self-fulfilling prophecy that these meetings did not include substantial numbers of *S. pombe* presentations.

The first significant international gathering of fission yeast scientists, organized by Jürg Kohli and Peter Munz, took place in Berne, Switzerland, in 1983 to celebrate Leupold's 60th birthday. In addition to members of the Institute of General Microbiology, >30 scientists from 9 countries attended to celebrate with the father of *S. pombe* genetics. Three years later, a 2-day pre-meeting workshop on fission yeast was held in Calgary, Canada, in conjunction with the Thirteenth International Conference on Yeast Genetics and Molecular Biology at Banff. This gathering included ~50 *S. pombe* scientists from 14 countries, with most of the participants having the opportunity to talk about their research (Coddington *et al.* 1987). Along with enhancing direct interactions among the various fission yeast labs, this meeting helped to establish the rules for *S. pombe* genetic nomenclature (Kohli 1987) and

served as the basis for the first book that gathered together much of our understanding of *S. pombe* at the time (Nasim *et al.* 1989).

The 1986 workshop in Calgary also led to the establishment of a fission yeast course as part of the Cold Spring Harbor Laboratory course series. The precise origin of the course is not clear, but it seems that Beach was responsible for the original idea, which was further discussed by Hyams, Fantes, Young, and others. Beach, Hyams, and Fantes were the instructors on the first run of the course in 1989. Maureen McLeod (Figure 1) was also a *de facto* organizer of this course by the time it came into being.

Meanwhile in Europe, a Molecular Genetics with Fission Yeast course was developed by Egel, Nurse, and Olaf Nielsen (Figure 1) as part of the European Molecular Biology Organization Practical Course series. The course was first given in 1994 in Copenhagen. It has continued to be taught every 2 or 3 years in Copenhagen and then more recently in Manchester, England, and Paris.

In addition to these courses, three workshops were given at GSA Yeast Genetics Meetings in 1996, 1998, and 2000 (this one focused on both *S. pombe* and *Candida albicans*). The first of these was organized by Young, Hoffman, and Susan Forsburg and came about due to Young's presence on the GSA Organizing Committee. These workshops gave the participants an opportunity to present their research specifically to their fission yeast colleagues and to discuss new reagents and methods that were being developed to advance molecular genetic research. It also gave participants a chance to put faces to the names they encountered on the USENET newsgroup http://www.bio.net/bionet/mm/yeast/.

By the late 1990s, it had become clear to Nurse that the *S. pombe* research community had grown large enough to sustain its own organismal meeting. He recruited Yanagida to serve with him as the Program Organizers and Stuart MacNeill (former Nurse Ph.D. student and Fantes postdoc) to serve as the local Organizer for the First International Fission Yeast Meeting. This was held in Edinburgh in September 1999 (Partridge and Allshire 2000). The Introductory Session featured talks by Nurse, Mitchison, Egel, and Yanagida, along with a letter from Leupold (read by Nurse). There were >440 attendees who presented >300 talks and posters. These scientists came from nearly 160 laboratories, 28 countries, and six continents (Table 1). Based on the history of *S. pombe* research and the investments that various countries have made in basic research, it is not surprising to see that the three most highly represented countries were the United States, the United Kingdom, and Japan. What was somewhat unexpected has been the popularity of *S. pombe* research in Spain (Table 1). In fact, even today there are eight different research groups in Salamanca (Sergio Moreno, personal communication), which may be second only to Tokyo for the number of *S. pombe* labs in a single city (Kunihiro Ohta, personal communication), although not in terms of labs per capita.

While nearly everyone who has contributed to the growth of *S. pombe* as a model research organism has been an academic researcher, one person stands out as a talented engineer and businessman. The late Carl Singer (Figure 1), whose company Singer Instruments produces equipment for yeast genetic research, attended many *S. pombe* courses and conferences with his range of technology for dissecting tetrads and, later, robots for handling large numbers of strains. Carl's cheerful presence and friendly insistence that *anyone* could learn to dissect tetrads was a feature of the Cold Spring Harbor Laboratory courses, besides which he ensured a steady supply of beer to the participants. He is sadly missed, although the presence of Singers at *S. pombe* and other yeast meetings continues on through his brother Jan and his son Harry.

The success of the 1999 meeting in Edinburgh led to the creation of a biennial conference the location of which rotates from Europe to Japan to North America. To date, there have been eight conferences (Edinburgh, Kyoto, San Diego, Copenhagen, Tokyo, Boston, London, and Kobe), with a 2017 meeting planned for Banff, Canada. These international conferences have been complemented by a variety of regionally based meetings of *S. pombe* workers and the development of the PomBase Model Organism Database (Wood *et al.* 2012; Hoffman *et al.* 2015; McDowall *et al.* 2015). All testify to the growth in importance of *S. pombe* as a model organism to

Table 1 Country of origin of *S. pombe* labs at 1999 Edinburgh meeting

Continent/country	No. of labs
Europe	
United Kingdom	30
Spain	10
France	7
Germany	6
Switzerland	5
Hungary	3
Denmark	2
Finland	2
Norway	2
Belgium	1
Czech Republic	1
Ireland	1
Poland	1
Russia	1
Slovenia	1
Sweden	1
The Netherlands	1
Turkey	1
Asia	
Japan	25
Israel	2
Korea	2
India	1
Singapore	1
North America	
United States	40
Canada	6
South America	
Brazil	1
Africa	
South Africa	1
Australia	1

biomedical science over the past 70 years, leading to new areas of research including RNA interference and related research that has recently established *S. pombe* as an important organism for the study of chromatin regulation and epigenetics (see the *Notable Advances from Research on Fission Yeast* section of Hoffman *et al.* 2015). These new research topics along with the development of new tools to study *S. pombe* biology, such as the construction of collections of haploid strains carrying viable deletion alleles or of diploid strains carrying heterozygous gene deletions (Kim *et al.* 2010), will drive the continued growth of *S. pombe* as a model organism for many years to come.

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