Michael G. Rossmann passed away in the early morning of May 14, 2019, after a long and fearless battle against cancer. Michael was a great scientist and a giant in structural biology and structural virology. He was also a long-time member of the Editorial Board at Structure. His accomplishments were recognized by numerous honors and awards, including election to the US National Academy of Sciences (1984), the Louisa Gross Hortwitz Prize (Columbia University, 1990), and the Gregori Aminoff Prize (Royal Swedish Academy of Sciences, 1994).

Michael was born in Frankfurt, Germany in 1930. In 1939, as a young Jewish boy, Michael traveled to England to visit his relatives just before World War II broke out and fortunately escaped from possible Nazi persecution (Kleine-Ahlbrandt, 2001). Michael received his BSc and MSc degrees from the University of London, majoring in mathematics and physics. Since high school, and influenced by Kathleen Lonsdale (Rossmann, 1999), Michael had strong interests in crystallography; starting from 1953, Michael pursued his PhD in the field of chemical crystallography with J. Montteath Robertson at the University of Glasgow while teaching physics in a technical college (Rossmann, 1999). After graduation in 1956, Michael came to the US as a postdoctoral fellow in William Lipscomb’s laboratory at the University of Minnesota, working on structures of terpenoids. There, Michael learned programming and used computers to help solve structures.

As it turned out, writing and debugging programs became one of the things that Michael most enjoyed doing, to the last days of his life. Together with his strong background in mathematics, physics, and crystallography, Michael wrote numerous programs for crystallography, including data processing, isomorphous replacement phasing, molecular replacement, and non-crystallographic symmetry averaging. Moreover, the theoretical considerations and methodologies he implemented in these programs became the foundation in most of the current programs for structural biology. Interestingly, Michael never learned the formal touching method; therefore, all of his programs, amounting to several hundred thousand lines of computer codes, were typed using primarily his right index finger!

In 1957, after listening to a lecture by Dorothy Hodgkin about protein crystallography, Michael was deeply attracted to this challenging field, and decided to move back to the UK to do his second post-doctoral training with Max Perutz at the MRC (Medical Research Council) Unit for Molecular Biology (later the Laboratory of Molecular Biology), which was a new branch of Cavendish Laboratory at the University of Cambridge. His computer skills contributed significantly to the structure determination of hemoglobin, especially in solving the phase problem using the method of heavy-atom isomorphous replacement.

It was in the hemoglobin project that Michael realized the structural similarity between its $\alpha$ and $\beta$ subunits could be used for Patterson function analyses in solving the phase problem, which eventually led to the development of the molecular replacement (MR) method (Rossmann and Blow, 1962). It is a very interesting coincidence that MR is also Michael’s initials. MR is now used in more than 85% of structures determined by X-ray crystallography. It was also because of this project that Michael became keenly interested in searching for structural similarity. After he learned about the new hypothesis from Watson and Crick that small viruses are constructed from identical subunits packaged in a regular way, Michael realized that viruses would be perfect samples for using MR. It is noteworthy that during this time, solving the structure of the 64 kDa hemoglobin was already a technical challenge; targeting virus structures that can be 100 times larger using X-ray crystallography was viewed as a “crazy” or “suicidal” direction.

Nevertheless, Michael bravely started his new adventure into virus structures. When he moved to the US again and established his own laboratory at Purdue University in 1964, his first NIH grant proposal was titled “X-ray Determinations of Proteins and Viruses” (Rossmann, 1999). Keeping his mind on virus structures, Michael first worked on some enzymes that had multiple identical subunits such as the lactic dehydrogenases. Michael’s keen interest in structural similarity again led to his discovery of a conserved pattern of secondary structures in many different types of dehydrogenases. Michael called these patterns “super-secondary structures” (Rao and Rossmann, 1973), which later evolved into the concept of “motif” or “fold.” The nucleotide binding motif discovered in these dehydrogenases was named after Michael as the “Rossmann fold,” which turned out to be one of the most abundant folds in nature.

After testing his idea on the multi-subunit enzymes, in the late 1970s, Michael finally was able to tackle his dream project on viruses, starting first with small plant viruses such as the southern bean mosaic virus. In 1985, Michael solved the structure of human rhinovirus (Rossmann et al., 1985), a major breakthrough for understanding viral diseases at the molecular level. In addition, collaborating with virologists who studied antibody escape mutants, Michael proposed his “canyon
determining virus particle orientations in crystals (Tong and Rossmann, 1990), and solvent flattening and phase extension using non-crystallographic symmetry (Rossmann, 1990), all of which are widely used in the field today.

Michael was among the first X-ray crystallographers who realized the power and potential of cryo-electron microscopy (cryo-EM). Michael did sabbaticals and attended many workshops learning from younger scientists about cryo-EM. With his efforts, Purdue became one of the early centers where cryo-EM and X-ray crystallography were combined to study many virus-related structures. Michael himself wrote the EMfit (Rossmann, 2000) program to dock atomic structures into low resolution cryo-EM maps, at that time to generate pseudo-atomic structures. As many tools were developed for virus structural studies, Michael’s interests expanded from plant viruses and picornaviruses to many different viruses include bacteriophage, flaviviruses, and giant DNA viruses.

Michael always believed that science should be pure and only driven by curiosity. When companies wanted to buy the atomic coordinates of the human common cold virus, Michael released the structure to the public. When other structural virologists were more in favor of working on disease-related viruses, Michael was always very proud of his bacteriophage work such as the T4 phage structure. Once a lab member asked him why not work on some “hot” (popular) viruses: Michael replied that he would work on the “cold” projects and make them “hot.”

While fighting cancer during his last years, Michael was still very active in his research projects, including those with many of his long-time collaborators. Michael solved the Zika virus structure together with Richard Kuhn, published a near-atomic structure of a giant virus with James Van Etten, and worked on a new idea of using cryo-EM to detect mutations in bacteriophage with Bentley Fane. Even during his last conscious moments, he still talked about what he would do after he recovered and returned to the lab. Another project that occupied his mind was a new, third edition of Volume F of the International Tables for Crystallography. In 2001, Michael and Eddy Arnold initiated the first edition of this volume on crystallography of biological macromolecules. He was planning the third edition together with Eddy Arnold and Liang Tong, and this new edition will be dedicated in his memory.

Michael had a keen interest in other cultures. His laboratory routinely had scientists from all over the world, and he always talked to all of his trainees to learn about their different cultures. His trainees are now spread all over the globe. Michael also traveled tirelessly around the world, presenting his research, teaching structural biology, and sharing his enthusiasm for science, even in his last year at the age of 88 and after two sessions of chemotherapy. In fact, Michael’s passion for science was legendary and he did truly live for science. For those of us who had the opportunity to work in his laboratory or collaborate with him, we observed it firsthand and were deeply affected by it. For all of us who had the opportunity to listen to one of his talks, that enthusiasm was immediately apparent, and infectious.

Besides science, Michael was also full of energy for life, especially in the three hobbies that he was most fond of: hiking, sailing, and skiing. At the many conferences he attended, whenever possible, he would go on hikes. His walking speed was faster than many of his younger colleagues. Until his last several years, Michael walked to the office in the morning on most days. It was a 45-minute walk from his home to the office. In addition, on his way to the office, he would climb up the stairs of the Purdue Math Building (the tallest building on campus) to prepare himself for the mountain hiking trips that he took almost every year. Sailing was a hobby that Michael started during his time in the UK. He was a beloved member of the local sailing club, where he had won many championships. He was very competitive when sailing and eager to learn any tricks to speed up the boat. He would become very frustrated when his boat fell behind other boats. Influenced by Max Perutz, Michael loved skiing and was highly enthusiastic about it (Figure 1). Because of that, many accidents (and unfortunately some injuries) and interesting stories happened to Michael on the ski slopes, until the doctor strongly advised him not to go skiing again in his 80s, as it might...
complicate his cancer therapy. Michael always complained to his children, his trainees, and his friends that his ski skills were not as good as before, never thinking about his age. As a testimony of his full energy and full curiosity of life, Michael still sailed and biked in 2015, kayaked in 2016, and in 2017, at the age of 87 and fighting cancer, Michael insisted on trying hoverboard.

Looking back at Michael’s scientific career, from small molecules to protein structures, from enzymes to giant virus structures, he always took those challenges that many other researchers thought were impossible. Some of his ideas and methods such as molecular replacement and phase extension using non-crystallographic symmetry were strongly doubted by his peers at the beginning but later became his major contributions to science. His passing is an immeasurable loss for structural biology, structural virology, and the scientific community in general. For us, as in one of Isaac Newton’s famous quotes, Michael will continue to live in our memory as a forever inquisitive boy playing on the beach finding smoother pebbles or prettier shells than ordinary (Figure 2).

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