

In Memory of Michael Rossmann: Scientist, Mentor, and Friend



Tom Blundell, Eddy Arnold, and Michael Rossmann Erice, Sicily 2006

Michael Rossmann's Amazing Years at Cambridge

- Worked with Max Perutz to solve hemoglobin structure
- Established general methodology for isomorphous replacement and anomalous dispersion phasing, Difference Patterson maps
- Developed molecular replacement method to solve 85+% of protein structures nowadays, and use of symmetry

Rossmann, M.G., "The Accurate Determination of the Position and Shape of Heavy-Atom Replacement Groups in Proteins," *Acta Cryst.*, **13**:221-236, 1960.

Rossmann, M.G., "The Position of Anomalous Scatterers in Protein Crystals," *Acta Cryst.*, **14**:383-388, 1961.

Blow, D.M. and Rossmann, M.G., "The Single Isomorphous Replacement Method," *Acta Cryst.*, **14**:1195-1202, 1961.

Rossmann, M.G. and Blow, D.M., "The Refinement of Structures Partially Determined by the Isomorphous Replacement Method," *Acta Cryst.*, **14**:641-647, 1961.

Rossmann, M.G. and Blow, D.M., "The Detection of Sub-Units within the Crystallographic Asymmetric Unit," *Acta Cryst.*, **15**:24-31, 1962.

Perutz, M.F., Rossmann, M.G., Cullis, A.F., Muirhead, H., Will, G., and North, A.C.T., "Structure of Haemoglobin: A Three-Dimensional Fourier Synthesis at 5.5-Å Resolution, Obtained by X-Ray Analysis," *Nature*, **185**:416-422, 1960.

Technological Innovations in Solving the Common Cold Virus Structure

- Scale-up of human rhinovirus 14 production (Rueckert, Erickson)
- Synchrotron, supercomputer, 20-fold averaging in P2₁3 cubic crystals
- Most convincing application of gradual phase extension from 5 to 3.5 Å resolution using non-crystallographic symmetry averaging and reconstruction
- Perfect phases from NCS averaging were used as observations in atomic model refinement (using adapted version of PROLSQ)

Arnold, E., Erickson, J.W., Fout, G.S., Frankenberger, E.A., Hecht, H.J., Luo, M., Rossmann, M.G. and Rueckert, R.R., "Virion orientation in cubic crystals of the human common cold virus HRV14," *J. Mol. Biol.*, **177**:417-430, 1984.

Arnold, E. and Rossmann, M.G., "Effect of errors, redundancy, and solvent content in the molecular replacement procedure for the structure determination of biological macromolecules," *Proc. Natl. Acad. Sci. USA*, **83**:5489-5493, 1986.

Rossmann, M.G., Arnold, E. and Vriend, G., "Comparison of vector search and feedback methods for finding heavy-atom sites in isomorphous derivatives," *Acta Cryst.*, **A42**:325-334, 1986.

Vriend, G., Rossmann, M.G., Arnold, E., Luo, M., Griffith, J.P. and Moffat, K., "Post-refinement of oscillation diffraction data collected at a synchrotron source," *J. Appl. Cryst.*, **19**:134-139, 1986.

Arnold, E., Vriend, G., Luo, M., Griffith, J.P., Kamer, G., Erickson, J.W., Johnson, J.E. and Rossmann, M.G., "The structure determination of a common cold virus, human rhinovirus 14," *Acta Cryst.*, **A43**: 346-361, 1987.

Arnold, E. and Rossmann, M.G., "The use of molecular-replacement phases for the refinement of the human rhinovirus 14 structure," *Acta Crystallogr.* **A44**:270-282, 1988.

Rossmann, M.G. and Arnold, E. 2.3. Patterson and molecular-replacement technique, In: *International Tables for Crystallography*, S. U., eds., 230-263. Reidel Publishing Co., Dordrecht; 1993

Remarkable Biology of a Common Cold Virus

Complete atomic structure of an animal virus!

(Poliovirus: Hogle, J.M., Chow, M., and Filman, D. *Science*, 229:1358-1365, 1985)

Receptor attachment: "The Canyon Hypothesis"

Location of neutralizing antibody binding sites (Sherry, B. and Rueckert, R.R.)

Evolution: same coat protein fold for plant and animal viruses (MGR's leitmotif!)

Drug binding and site of attachment, basis for drug design

Smith, T.J., Kremer, M.J., Luo, M., Vriend, G., Arnold, E., Kamer, G., Rossmann, M.G., McKinlay, M.A., Diana, G.D. and Otto, M.J., "The site of attachment in human rhinovirus 14 for antiviral agents that inhibit uncoating," *Science*, **233**:1286-1293, 1986.

Implications for assembly, including polyprotein processing

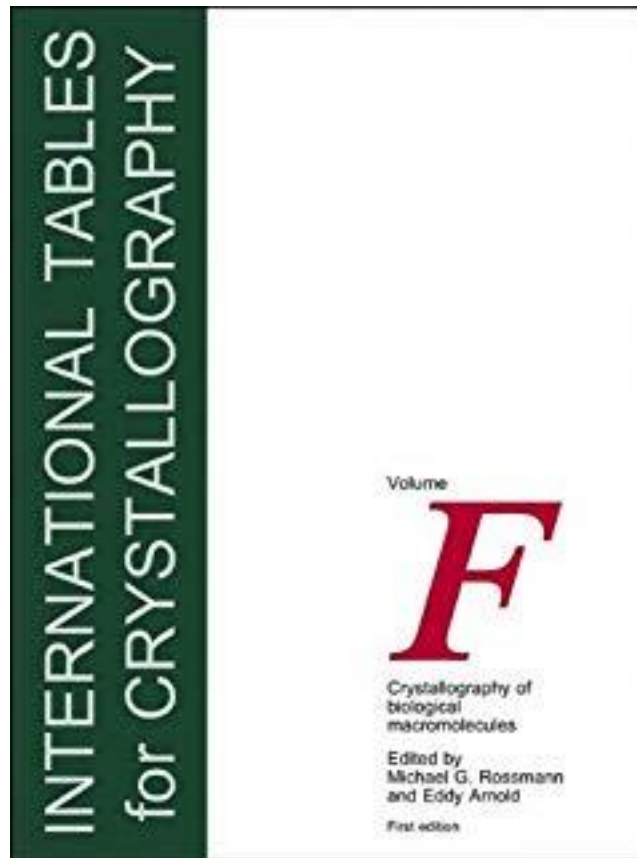
Arnold, E., Luo, M., Vriend, G., Rossmann, M.G., Palmenberg, A.C., Parks, G.D., Nicklin, M.J.H. and Wimmer, E., "Implications of the picornavirus capsid structure for polyprotein processing," *Proc. Natl. Acad. Sci. USA*, **84**:21-25, 1987.

Structure of a human common cold virus and functional relationship to other picornaviruses

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1st edition: 2001 M.G. Rossmann and E. Arnold, Editors

2nd edition: 2012 E. Arnold, D.M. Himmel, and M.G. Rossmann, Editors

3rd edition: 2022 L. Tong, M.G. Rossmann, and E. Arnold, Editors*

*** -dedicated to Michael**



An inspiration for so many!

Michael with Arnold lab group, January 2017



A close family friend

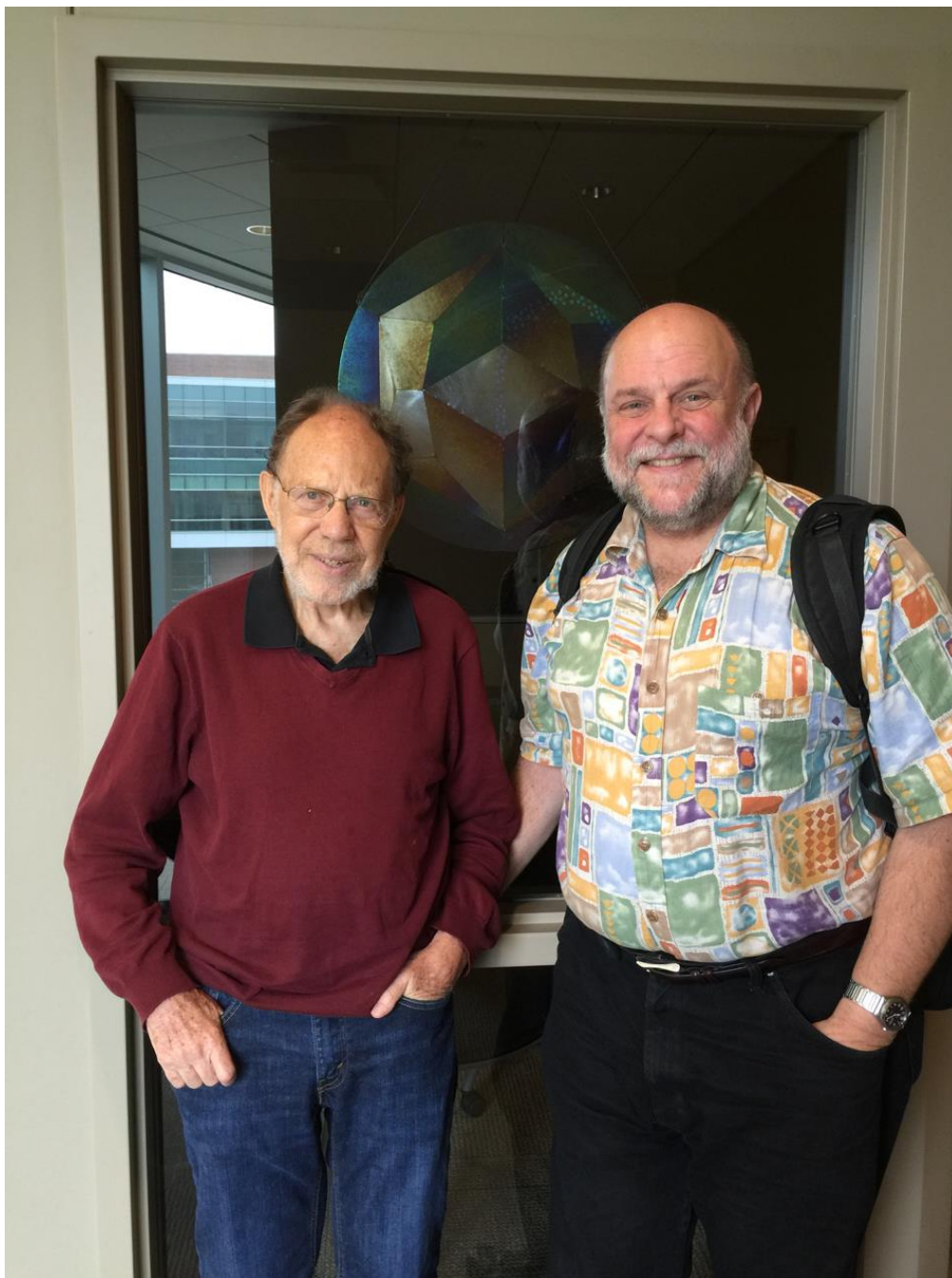
Macatawa, on Lake Michigan, August 2016



Shatkin Lecturer Michael with Eddy Arnold and Karen Bogan, Rutgers, November 2018



Michael with Louise Arnold and Stephen Burley, New Jersey, November 2018



Thank you Michael!

Hockmeyer Hall,
Purdue
October 2014

Reflections on Michael's career strategy: the 10,000 hour theory

- Observations (Malcolm Gladwell, “Outliers” and others) suggest that it takes ~10,000 hours of concentrated, organized, and deliberate training to become an expert in various fields

a chess grandmaster

a top-tier concert pianist

- Why not apply this concept to science?

- Estimate: Michael invested >200,000 hours in his scientific research!

The combination of natural abilities, skill, training, and continuous passion for research paid off—just some of the many factors that made Michael a spectacular scientist and wonderful mentor to so many of us

- Michael's students: 15,000,000 hours? 5,000 person-years??