Learning in the Lockdown: Free Online CryoEM School

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Many structural biologists have had less time to do experiments during the coronavirus pandemic, and are stuck at home with no access to the lab. During the Great Plague of London, Isaac Newton had to work from home, too. Cambridge University sent their students home, and he had an annus mirabilis (year of wonders) on his family estate. While we may not manage to have Eureka moments in calculus, optics and gravity, as this physicist did, we can still make lemonade from lemons because learning the math and theory of cryoEM requires no access to the bench!

In the spirit of solidarity during the pandemic, I launched a free online cryoEM study group in November 2020, and have received over 300 registrations from trainees, long term staff, and principal investigators. How much math and theory do cryoEM structural biologists need or want to know, either for solving structures or developing novel methods? Determining the 3D structure of biomolecules from noisy 2D projections involves advanced mathematical concepts, as well as implementation issues in working with discrete pixelated data. Practitioners often lack an understanding of what is happening inside during data processing. However, many practitioners have a desire to open up the "black box", become an expert at data processing, and better interpret the biological meaning of 3D reconstructions. As one respondent put it "I am interested in being more than a button pusher".

The learning style is largely a flipped classroom, with pre-lecture readings such as the wonderful free online courses already available provided beforehand. We spend online meetings answering questions, working out problems, and building intuition between data, equations, code, and experimental and data processing choices.

We have had half a year of weekly meetings on topics like complex numbers, Fourier transforms, phase contrast imaging, Nyquist, expectation-maximization, rotations, interpolation in 3D, reconstruction by Fourier inversion, variational autoencoders, normal mode analysis, preferred orientations. Future work includes guest lectures on the multislice forward model, 3D principal component analysis, as well as learning from interactive coding notebooks that illustrate commonly encountered problems in data processing and how to diagnose them and troubleshoot with simple examples.

A syllabus, annotated bibliography, and online coding notebooks can be found at
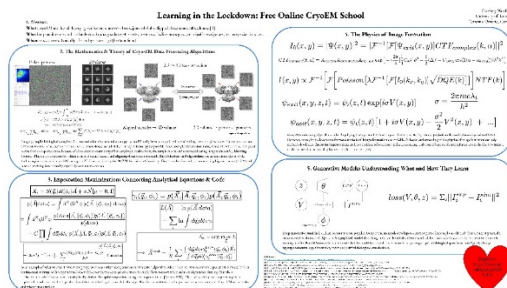https://github.com/geoffwoollard/learn_cryoem_math,

Figure 1