Draft Agenda (7/30/2017)

Workshop on Advanced Topics in EM Structure Determination: Challenges and Opportunities.

October 29 - November 3, 2017.

National Resource for Automated Molecular Microscopy
Simons Electron Microscopy Center
The New York Structural Biology Center

[We encourage presenters to address the questions posed below. We ask presenters not to give their usual seminar; we would prefer a broader context for discussion of the issues. Presentations need not and should not be limited to the lecturer's own work. Summarizing the current state of the art (with examples), followed by identification of present challenges and possible opportunities to address issues, is a good overall plan for most lectures. We do not expect presenters to have all the answers and we encourage plenty of questions and discussion both during and after the talks.]

Sunday October 29 **Theme: Setting the Scene**

Session Chair: Clint Potter

4:00 pm ***Registration opens***

4:45 pm **Welcome** **Bridget Carragher, Clint Potter**

Session Chair: Clint Potter

[These two introductory talks serve to set the scene and introduce the topics for more in depth discussion in the following days.]

5:00 pm **Challenges and Opportunities for Molecular Structure Determination**
Yifan Cheng

[This introductory talk will describe the big picture: what have we achieved and what do we still need to do. Near atomic resolution single particle structure are now almost routine for well behaved samples. What are the remaining challenges and limitations. Why does this not work for every sample? Why is the resolution still limited for most samples? Are there any general principles that might be applied to "difficult" specimens? Are there well-established best practices for imaging and data processing? How often do these need to be modified? When should we use energy filters, phase plates, Cs correctors, super resolution? What are the challenges in looking at intermediate states? Where should we focus our efforts in the immediate future? What should we pay attention to and what should we NOT do?]

6:00 pm **Challenges and Opportunities for Cellular Structure Determination**
John Briggs

[This introductory talk will describe the big picture: what have we achieved and what do we still need to do. How important is it to visualize complexes in their biological environment? What classes of biological questions are best addressed this way? What are the problems associated with imaging large cellular complexes in situ? How do we

locate and identify what we are interested in? How important is correlative LM-EM? Has this approach reached a stage of development where it is easily and generally applicable? What are the challenges associated with recording high-resolution information from cells? What are the general strategies currently in use? What is the role of FIB milling and other advanced specimen preparation methods? What technologies do we still need? Is tomography coupled with sub tomogram averaging the best way to extract the highest resolution information? This approach has recently yielded near atomic resolution structures; could this become routine? Are there theoretical limitations to what can be achieved? What is the current state of the art and the future prospects? What should we pay attention to and what should we NOT do?]

7:00 pm Opening reception

Monday October 30 Theme: Specimen preparation

8:00 am Breakfast

Session Chair: Tom Walz

9:00 am Challenges remaining for specimen preparation
Bob Glaeser

[Here we would like to expand on specimen preparation issues introduced in the previous day's talks. Most specimens are still not ready for atomic resolution. What are the specific and general problems? What can be done about them? Which approaches have been tried in the past? How successful have they been? Which approaches look like the most promising?]

10:15 am Coffee Break

10:45 am New approaches to substrates and specimen preparation.
Chris Russo

[Are there treatments that can be applied to thin carbon that are advantageous? Should we be using carbon at all? Are there new substrates that offer advantages over the traditional thin carbon? Can we envision improving on these further using surface treatments?]

11:20 am Spotiton and nanowire grids TBA

[Do new approaches to specimen preparation improve quality and throughput? Can we produce thin layers reproducibly? What are the limitations? What else can be done?]

12:00 Lunch and group photo

1:00 pm Single cell imaging Henning Stahlberg

1:30 pm CryoET as a method to understand the air-water interface
Alex Noble

2:00 pm TBA TBA

2:30 pm Coffee Break

3:00 pm Demos / Vendor breakout sessions / User breakout sessions

[These parallel sessions will involve demonstrations of microscope and cameras, specimen preparation equipment, major software applications, meetings of users

groups. Some of these sessions will go on all week and we will have sign up sheets for some of the small group demonstrations that will occur multiple times to ensure that everyone gets a chance to attend the ones they are interested in.]

4:00 pm Panel Discussion: Tom Walz (Chair)
[For these panel discussions, all participants are encouraged to submit questions before or during the meeting that will then be discussed in an open forum. Questions are preferably related to topics on which presentations have already been made and should expand on or clarify the lectures of the day. The Chair is encouraged to plant some seeds in the audience to get the discussion going.]

5:00 pm Poster Session
[Posters will be displayed in three sessions (probably separated alphabetically). The poster session is one of the most interactive and valuable aspects of the meeting. Refreshments will be served during the poster session.]

6:30 pm Dinner

7:30 pm Talk TBA
[This talk should highlight the biological results while also drawing attention to the technical advances that made it possible.]

Tuesday October 31 Theme: Image acquisition

8:00 am Breakfast

Session Chair: Bridget Carragher

9:00 am Optimizing image acquisition John Rubinstein
[How to get the most out of your microscope and your direct detector. Details of the methods, formulae, math and common sense needed for optimal data collection.]

10:15 am Coffee Break

10:45 am Phase plates Rado Danev
Are these the key to high resolution of small and heterogeneous particles? Can we make them easier to use? What are the remaining issues with using them? Will there be new progressing the near future for these devices?]

11:30 am Next generation cameras.
Paul Mooney
Scott Stagg

[What does the future hold for improvements in detectors.]

1:00 pm Boxed Lunch To Go

Wednesday November 1 Theme: Processing

8:00 am Breakfast

Session Chair: Joachim Frank

9:00 am Introduction and new approaches Sjors Scheres
[A comprehensive overview of the major advances that have taken place in the last few years that have enabled 3D maps to achieve "atomic" resolution. Topic to be covered include: 3D reconstruction, image restoration techniques, how to deal with heterogeneous populations. What are the hot topics in processing? What are the major mathematical approaches and available software? What are the success stories and the failures? Where are the greatest challenges right now and how are we approaching these? Do we need completely new algorithms or just incremental improvements on the current ones? Mistakes to avoid! Some of these topics will be shared between this talk and the next two, the presenters are encouraged to discuss this and make a plan.]

10:00 am Coffee Break

10:30 am New challenges Niko Grigorieff
[It seems that one of the greatest challenges now will be sorting out heterogeneity in 3D. How do we detect heterogeneity and make sure it does not lead us to the incorrect result? What are the signs that it is present in a dataset? How to distinguish conformational vs. compositional variability? What are the prospects for really getting to atomic resolution for a small and heterogeneous particle? Under what circumstances can we hope to be able to do this? Are there some samples that will never be amenable to high resolution reconstruction?]

11:15 am Deep learning methods Steve Ludtke
[Discussion on what we still need to do in terms of providing the computational tools needed by the community to do 3D EM in a routine and reliable manner. Discussion of new algorithms both for separating heterogeneous populations and for more accurate orientation determination.]

12:00 Lunch

1:00 pm Short talk

1:30 pm Short talk

2:00 pm Panel Discussion
[For these panel discussions, all participants are encouraged to submit questions before or during the meeting that will then be discussed in an open forum. Questions are preferably related to topics on which presentations have already been made and should expand on or clarify the lectures of the day. The Chair is encouraged to plant some seeds (moles) in the audience to get the discussion going.]

3:00 pm Coffee Break

3:30 pm Poster session
[Posters will be displayed in two sessions (probably separated alphabetically). The poster session is one of the most interactive and valuable aspects of the meeting. To maximize the space available for the poster session we plan to display the posters on the walls of the microscopy suite building and they will need to be attached to the wall using very discrete Velcro sticky back coins on the back of the poster.]

5:00 pm Manufacturers Exhibit
[Several manufacturer's have agreed to provide one-on-one or small group demonstrations using the microscopes and cameras in the Hazen Suite during the exhibit hours. To arrange a demonstration please contact the manufacturer

representatives attending the meeting or stop by the exhibit and talk to them directly.]

6:30 pm Dinner

7:30 pm Research Talk Jue Chen
[This talk will highlight the biology while also drawing attention to the technical advances that made it possible.]

Thursday November 2 Theme: Challenges and Opportunities

8:00 am *Breakfast*

Session Chair: TBA

9:00 am Challenges and Opportunities: SP Wah Chiu
[Validation methods have become much better established over the last couple of years. What are the methods that are being used? In what resolution realms are they useful? Do we need more tools? How do we avoid mistakes? Is validation at very high resolution easier than at intermediate resolutions? What about highly heterogeneous datasets?]

10:15 am Coffee Break

10:45 am Challenges and Opportunities: CryoET Elizabeth Villa

11:30 am Fitting challenges David Veesler
[Methods for fitting backbone tracing into moderate resolution structures. What are the problems, how are they approached, what are the solutions. How do we validate the methods and the resutls?]

12:00 Lunch

1:00 pm 3 short talks TBA

2:30 pm Demos / Vendor breakout sessions / User breakout sessions
[These parallel sessions will involve demonstrations of microscope and cameras, specimen preparation equipment, major software applications, meetings of users groups. Some of these sessions will go on all week and we will have sign up sheets for some of the small group demonstrations that will occur multiple times to ensure that everyone gets a chance to attend the ones they are interested in.]

3:30 pm Coffee Break

4:00 pm Poster session
[Posters will be displayed in two sessions (probably separated alphabetically). The poster session is one of the most interactive and valuable aspects of the meeting. To maximize the space available for the poster session we plan to display the posters on the walls of the microscopy suite building and they will need to be attached to the wall using very discrete Velcro sticky back coins on the back of the poster.]

6:00 pm Conference dinner

Friday November 3 **Theme: Putting theory into practice**

8:00 am ***Breakfast***

Session Chair: Clint Potter

[This session is targeted at relatively newcomers to the field and thus we do not expect all attendees to stay for this, only those with a particular interest in the topics to be covered. We plan to spend the morning on presentations that are focused on practical aspects of doing cryoEM. What does it take to set up a lab? What are the pitfalls of specimen preparation? What instruments should you buy, beg borrow, or steal? What kind of computational resources are needed? What strategies are there available to cope with the onslaught of data resulting from the new generation of detectors. We are still considering the topics to be covered so let us know if you have suggestions. The format of the morning will be a series of short talks by experts in the field interspersed with lots of discussion.]

9:00 am **How to choose the optimal microscope/camera combinations.**
[What do you need? How do you validate your instrument performance? How many people does each microscope serve? How do you schedule time to optimize the instrument usage and performance?]
10 minutes each
TBA

9:45 am **The essentials of a cryoEM lab.**
[What do you need? What can you borrow? How do you validate your equipment? How do you service your equipment? How do you assess a new specimen?]
TBA

10:30 am ***Coffee Break***

11:00 am **Computational infrastructure.**
[Computation has become a major bottleneck. Data storage (and backup/archive) are major issues. What do you need? What do you buy? Are so called supercomputer centers of value? What about cloud computing? What software do you need up and running? How do you support the hardware and software? How do you validate the software?]
TBA

11:45 am **Wrapup**

12:00 ***Lunches To Go and End of Workshop***