This year the interest group meeting focused on discussing best practices, control experiments and data harmonization of the three areas covered in this group. Specific questions related to discussion topics were sent to interest group members through online forum a month before the workshop.

Three contributors gave ~10-minute presentations to give their expert views on best practices, control experiments and data harmonization followed by discussion of their topics with the audience. The presenters provided useful information for experts and newcomers. Ample time was devoted to an engaging discussion of each topic in turn. New and experienced researchers were able to ask questions and offer comments and suggestions. In general, participants found the meeting interactive and discussions interesting. Based on previous survey comments on insufficient amount of time for in-depth discussions for each of the three topics covered in this interest group, we asked the audience to vote on how to better organize our interest group in the future. As a result, more than 80% of attendees voted for requesting two consecutive sessions for the interest group next year.

The contributors were

Dr. Alexander Leitner, ETH Zurich.
Prof. David Schriemer, University of Calgary
Prof. Mark Chance, Case Western Reserve University

The questions of discussion were:

A. Cross-linking mass spectrometry
1. What would you recommend to newcomers to the field who want to start using cross-linking/MS?
2. Is there any way to find the best chemistry/software to use?
3. Where do you see opportunities for the application of cross-linking in industry, e.g. biopharma?
4. What/where are the limitations of current cross-linking approaches?
5. How to go from raw cross-linking data to structural information (modeling etc.)?
6. What is the current status for data standards, data deposition etc. for cross-linking/MS

B. HDX
1. Are we ready to standardize the analysis and reporting of HDX data?
2. Should we create a public repository for HDX data?
3. How well is HDX serving the biopharmaceutical industry?
4. Are we any closer to understanding the mechanism of exchange in structure? Will predicting exchange rates be possible?
5. What’s next in HDX-MS methods development?

C. Chemical labeling
1. What are best practices around how labeling dosimetry is conducted and made reproducible, both for continuing work and for novel systems never before explored. Determining extent of labeling is critical for reliable results.
2. How are results from covalent labeling validated? Mutagenesis, other biophysical approaches, etc.?
3. What visualizations are appropriate for showing covalent labeling data.
4. how can covalent labeling be integrated with other structural data?
2018 ASMS Interest Group meeting on HDX/CL/XL-MS

Focus for 2018:
Best practices, control experiments & data harmonization

Agenda:

1. Introduction (5 min)

2. XL-MS (20-25 min) – Alexander Leitner

3. HDX-MS (20-25 min) – David Schriemer

4. CL-MS (20-25 min) – Mark Chance

5. Round-up (5-10 min and very important vote!)
A few (personal) thoughts about the state of XL-MS:

• Diverse user base: MS/proteomics background, structural biology background

• Many different experimental workflows
  • Chemistry: Lys-specific, zero-length, photo-reactive, ...
  • Linker design: Cleavable, non-cleavable, isotope-coded, affinity-tagged, ...

• Applications of XL-MS span a wide range from single proteins to proteome-wide
  • De novo fold prediction (CASP)
  • Low accuracy restraints for integrative/hybrid modeling – (large) complexes
  • Large-scale interaction networks
  • Quantitative approaches for conformational changes
  • And more

• Huge number of software pipelines, commercial solutions start to emerge, no one size fits all solutions (for reasons listed above)
2018 ASMS Interest Group meeting on HDX/CL/XL-MS

A few (personal) thoughts about the state of XL-MS:

• Widely different reporting standards
  • Even most essential information is missing in many cases where XL was used as "auxiliary" technique
  • HUPO Proteomics Standard Initiative included limited support for XL-MS results in mzIdentML 1.2 (released 2017)
  • Slow uptake for deposition of XL-MS datasets in repositories such as PRIDE
  • XL data in PDB-dev (A. Sali) or cross-referenced?

• Community-based effort to get a first overview of experimental and computational strategies (A. Sinz, A. Leitner) using BSA as model protein – huge response, evaluation still in progress
  • Eventual aims: Suggest reporting standards and best practices, not find the best method
  • Needs to be extended to other targets relevant to the community (funding?)
XL-MS:

1. What would you recommend to newcomers to the field who want to start using cross-linking/MS?

2. Is there any way to find the best chemistry/software to use?

3. Where do you see opportunities for the application of cross-linking in industry, e.g. biopharma?

4. What/where are the limitations of current cross-linking approaches?

5. How to go from raw cross-linking data to structural information (modeling etc.)?

6. What is the current status for data standards, data deposition etc. for cross-linking/MS?
2nd International Conference on Hydrogen Deuterium Exchange Mass Spectrometry

May 21-24, 2019 (Banff, Alberta, Canada)

Session topics

• Integrative Structural Biology
• Protein Function
• Biopharmaceuticals/Drug Discovery
• Fundamentals/New Developments

www.hdxms.org
A uniquely powerful technique – the ultimate “reagentless” method

Applications (individual proteins to protein complexes)
- Conformations/folding
- Interactions (mapping/allostery)
- Stability (biotherapeutics)

Methodological diversity, but most of us use a bottom-up protocol (peptide-level deuteration analysis) as a routine method

A community-driven “recommendations” white paper in advanced stages!
• The challenges we face
  ➢ Reproducibility (control everything!)
  ➢ Transparency (report everything!)

• Needs/pressures/opportunities
  ➢ Publication standards?
  ➢ Central HDX data repository? (wwPDB on integrative structures https://pdb-dev.wwpdb.org/)

• Why we need each other (XL/HDX/CL)
  ➢ Interpretation!
  ➢ Eg: Need XL to understand HDX…and vise versa!
2018 ASMS Interest Group meeting on HDX/CL/XL-MS

HDX-MS:

1. Are we ready to standardize the analysis and reporting of HDX data?

2. Should we create a public repository for HDX data?

3. How well is HDX serving the biopharmaceutical industry?

4. Are we any closer to understanding the mechanism of exchange in structure? Will predicting exchange rates be possible?

5. What’s next in HDX-MS methods development?
CL-MS:

1. As labeling approaches have been improved and expanded, what are best practices around how labeling and dosimetry are conducted.

2. How are results from covalent labeling typically validated?

3. How can covalent labeling be integrated with other structural and biophysics data?

4. What new areas are ripe for application of CL technologies?
2018 ASMS Interest Group meeting on HDX/CL/XL-MS

Voting (to Brexit or not to Brexit...):

Vote 1:
- Should we keep the interest group meeting in the current format?

Vote 2:
- Should we separate into two distinct interest groups?

Vote 3:
- Should we keep the interest group as one but have two consecutive meetings (with different focus)?