Scholar Report

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Title of Scholarship Project: Advanced mass photometry for biomolecular characterization on supported lipid membranes

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Introduction to the Research

This project focused on the characterization of biomolecular dynamics and mass distribution on supported lipid bilayers (SLBs) using advanced mass photometry techniques. The primary aim was to develop a robust calibration approach enabling precise measurement of biomolecule mass and tracking their diffusion within a two-dimensional membrane environment.

The biomolecules studied in this research possess structural characteristics critical for biological functionality. Variations in these structures directly affect their biological roles, making precise mass and diffusion characterization valuable for future research in biological and medical sciences. Establishing a reliable, label-free method for biomolecule characterization could significantly enhance research capabilities, accelerating advancements in therapeutic and diagnostic applications.

Additionally, this project contributed methodological advancements in mass photometry, pushing the boundaries towards achieving single-molecule sensitivity for structurally complex biomolecules on lipid membranes. While further refinement is necessary, the foundational work completed during this project sets the stage for future studies.

Research Methods and Approach

Core Technique: Mass Photometry

The central method used in this project was mass photometry (MP), a technique utilizing interferometric scattering microscopy (iSCAT) to detect biomolecular binding events at interfaces. Advanced image processing techniques were implemented to significantly reduce noise and enhance image clarity. This approach allowed for the observation of individual biomolecules as detectable events, facilitating their visualisation and characterisation as they interacted and diffused on SLBs.

Experimental Design and Challenges

Supported lipid bilayers were meticulously prepared on glass substrates through extensive surface cleaning protocols, including chemical treatment (e.g., piranha solution) and UV-ozone processing. A specialized anchoring protein was employed to immobilize the biomolecules on SLBs in a controlled and reversible manner. This configuration allowed

biomolecules to be studied under near-native conditions without the interference of fluorescent or chemical labelling methods.

A key challenge was optimizing the image analysis and calibration methods required to accurately quantify biomolecular mass and track their lateral diffusion on lipid membranes. The iterative development of analytical algorithms was technically demanding, requiring dedicated sessions for adjustments and validation. Managing these iterative refinements alongside actual experimental data collection presented logistical and practical challenges yet was essential for achieving accurate and reproducible results. Although ongoing refinement is needed, significant methodological progress was made, establishing valuable groundwork for future research.

Impact and Significance of Research

Scientific and Medical Relevance

Developing precise and label-free methods for biomolecule characterization has considerable implications for various scientific and medical fields. Reliable and rapid quantification of biomolecular mass distributions may eventually facilitate advancements in diagnostics, therapeutics, and fundamental biological research. Moreover, the simplicity and speed of this approach make it potentially accessible and beneficial for broader scientific applications, enabling research groups worldwide to adopt advanced biomolecular analyses with minimal sample perturbation.

Broader Contributions to Methodological Development

Beyond biomedical applications, this project's methodological innovations contribute directly to expanding the utility of mass photometry. The developed calibration methodology and improved noise-reduction techniques enhance the capability of mass photometry to study molecular interactions on lipid membranes, broadening the range of biomolecular research applications.

Personal Development and Growth

1. Time Management and Strategic Decision-Making
Balancing analytical refinement with experimental data acquisition required careful planning, significantly improving my strategic decision-making and project management skills.

2. Refining Technical and Transferable Skills
The experience reinforced the importance of rigorous experimental design, detailed record-keeping, and systematic documentation, all crucial for reproducible and credible scientific research.

3. Navigating Scientific Challenges and Embracing Uncertainty
Adapting to unexpected experimental and technical challenges cultivated my resilience, patience, and flexibility, turning setbacks into valuable learning opportunities.

4. Building a Growth Mindset and Resilience
Working independently over an extended period enhanced my motivation, perseverance, and adaptability, supporting sustained personal and professional growth.

5. Collaborative Skills and Professional Confidence
Interactions with peers and supervisors within a supportive research environment helped develop effective communication, collaboration skills, and professional confidence, emphasizing the importance of teamwork in scientific research.

Impact on Future Goals and Aspirations

This research experience has significantly influenced my career aspirations. While I value the technical and methodological skills gained, the project underscored my preference for collaborative and dynamic environments, exemplified by my involvement in the Leeds University Rocketry Association (LURA), where interactive brainstorming and teamwork foster creative fulfilment.

Although pursuing a Ph.D. is not an immediate goal, this project clarified my professional strengths and interests within scientific research. I am now confident in my ability to contribute meaningfully to collaborative, multidisciplinary projects, aligning future pursuits with my strengths and interests.

Feedback and Reflections

Feedback from mentors highlighted my curiosity, engagement, and openness to collaborative scientific dialogue. Emphasizing that effective science thrives on supportive communities, this feedback reinforced my commitment to positive contributions in collaborative research settings.

Conclusion

This project provided transformative experiences, greatly enhancing my scientific, analytical, and professional skillsets. I am proud of contributing foundational methodological advancements in mass photometry for biomolecular characterization on lipid membranes. The technical, analytical, and collaborative skills developed during this project will be invaluable assets moving forward. Although the research area differs somewhat from my long-term career interests, the personal growth and insights gained will undoubtedly inform and enhance my future scientific contributions.

Supervisor Comments

Throughout his scholarship project, James has demonstrated a range of strengths that is impressive for an undergraduate student transiting from second to third year of studies. Most salient perhaps are curiosity and sharp-wittedness. From the very outset, James contributed with pertinent questions to supervisory meetings that demonstrated growing knowledge and out-of-the box thinking, and substantially contributed to shaping the project direction. In these meetings, and elsewhere, James showed excellent communication and team-working skills. With an open, respectful and inclusive attitude, he integrated with ease into my multi-disciplinary lab, and effectively communicated with physicists, chemists and biologists alike. James is very eager to learn and stress-tolerant. He also has a good ability to balance curiosity with critical thinking and improvisation, and to ask for help when needed. This enabled him to troubleshoot and progress effectively towards a set goal, and this with a high level of independence for his career stage.

If an area for further development is to be identified, then this would be James' record keeping. A structured and detailed record of data and results helps maximising impact, and James had a productive learning curve in this regard as the project evolved.

From the above brief appraisal, it should be clear the James demonstrated a set of leadership attributes during his project. He has potential to lead, for example, in terms of evidence-based decision-making, integrity, and capacity to motivate a wider team. These attributes will stand him in good stead for whatever career he decides to pursue. He clearly has the capacity to make an impact, be it in an academic or an industrial (and potentially even other) setting.

Signatures
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Date: 05/11/2024

Project Leader: Ralf Richter
Date: 06/03/2025