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<th>The Formation of Ice in Bacterial Fragments and their Biomimetics: Toward the Understanding of Biological Ice in the Atmosphere</th>
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**Project Highlights:**

- This is a truly multidisciplinary project spanning atmospheric science, physical chemistry and cryopreservation.
- The project features a unique blend of simulations and experiments, leveraging the cutting-edge facilities offered by the University of Warwick.
- There is the opportunity to make a real impact, by unravelling the microscopic details responsible for the formation of “biological ice” in the atmosphere – and in our own cells as well!
- This project can leverage a strong network of collaborations, particularly Dr. Thomas Whale (Leeds/Warwick, atmospheric ice nucleation) and Dr. Heather Knight (plant freezing tolerance).

**Overview**

The formation of ice is a process of paramount importance for atmospheric science, as it impacts the structure and the dynamics of e.g. mixed-phase clouds (Atkinson et al., 2013; Murray, 2017; Slater et al., 2015). Strikingly, water almost always needs the help of some foreign substance to transform into ice: while inorganic materials such as minerals or clays have been traditionally associated with the formation of ice (Kiselev et al., 2017), recent evidence indicates that biological systems such as bacterial fragments play a key role in facilitating the occurrence of "biological" ice in the atmosphere (Christner et al., 2008; Pratt et al., 2009; Hoose et al., 2010; O’Sullivan et al., 2015).

In fact, the formation of ice in biological matter is also crucial for cryopreservation and medical applications (John Morris and Acton, 2013; Jang et al., 2017) - and yet, we still do not know what is it that makes e.g. a certain bacterial fragment so efficient (or not!) in promoting the formation of ice. This is because the time- and length-scales involved with this process are awfully small/short (nano-seconds and nano-meters, respectively!) so that even state-of-the-art experiments struggle to achieve the necessary resolution we need to characterize this process.

In this project, we are going to unravel the origin of ice nucleation on bacterial fragments as well as some synthetic counterparts of them - some biomimetics (Congdon et al., 2015; Biggs et al., 2017), useful to pinpoint specific structural features of e.g. the cell walls. To this end, we will leverage a unique combination of computer simulations (Fitzner et al., 2019, 2015; Sosso et al., 2018) and...
experimental techniques (Deller et al., 2015; Casillo et al., 2017) spanning multiple time and length scales, from the atomistic details of hydrogen bonding to the ice nucleating ability of whole libraries of bacterial fragments, cell walls, and biomimetics.

This multidisciplinary approach harnesses the ice-related expertise of PI and Co-I, both based at the University of Warwick, to provide the student with an exceptional blend of skills, delivering a cutting-edge piece of research with the potential to transform our understanding of biological ice in the atmosphere. In addition, we envisage this proposal to also impact the current paradigm of cryopreservation, which relies on the challenging control of ice in our cells (Jang et al., 2017).

Figure 1: The aim of this project is to bring together computer simulations and cutting-edge experimental techniques to gain microscopic insight into the formation of ice in bacterial fragments – the prototypical biological system responsible for the formation of “biological” ice in the atmosphere

Methodology

This project features a mixture of simulations (Dr. Sosso, Co-I) and experiments (Prof. Gibson, PI).

Simulations of ice formation (nucleation and growth) (Fitzner et al., 2015; Sosso et al., 2018; Fitzner et al., 2019) in the presence of atomistic models of cellular membranes and cell walls will be performed by means of molecular dynamics simulations (Understanding Molecular Simulation, 2002). The relevant training and facilities will be provided by the research group of Dr. Sosso.

The molecular-level insight obtained will be leveraged to design splat assays (Deller et al., 2014) and frozen droplet experiments (Whale et al., 2015) aimed at quantifying the ice nucleating ability of different classes of bacterial fragments and selected biomimetics. These experiments will be performed under the supervision of Prof. Gibson.

Cryo-TEM as well as complementary biophysical techniques will also be used to gain further insight into the mechanism and kinetics of ice formation in bacterial fragments.

Training and skills

The project involves the usage of state-of-the-art experimental and computational techniques. On top of the CENTA training program, the research group of Dr. Sosso will provide specific training with respect to molecular simulations. The student will also be encouraged in year 1 to attend an international school offering a program focusing on computer modelling (e.g. the MolSim school: http://cecam-fr-moser.org/index.php/event/molsim-2019-understanding-molecular-simulation/). In
addition, the contribution of Dr. Whale to the project will provide bespoke training opportunities with respect to the frozen droplet experiments.

**Partners and collaboration**

This project can leverage a strong network of collaborations, particularly Dr. Thomas Whale (Leeds/Warwick, atmospheric ice nucleation) and Dr. Heather Knight (plant freezing tolerance). Broadly speaking, there is a lot of ice-related research going on in Warwick: PI and Co-I are already actively leveraging this expertise, and we expect this project to offer the possibility for the student to interact with a number of academic partners (Dr. Quigley [Physics], Dr. Smith [Life Sciences]). Industrial involvement is a possibility we are presently working on.

**Possible timeline**

*Year 1.* **Simulations:** Computer simulations of supercooled water at the interface with biomolecular systems representative of cell membranes and/or walls, such as functionalised lipid bilayers, sugar-coated molecular architectures. **Experiments:** culture/purification/synthesis of libraries of bacterial fragments and their biomimetics. **Training:** International school on molecular modelling.

*Year 2.* **Simulations:** Simulations of ice nucleation on biomolecular systems, using bespoke enhanced sampling techniques [see e.g. (Sosso et al., 2018)]. **Experiments:** frozen droplet experiments aimed to establishing the ice nucleating ability of different classes of bacterial fragments, guided by the molecular-level insight provided by the simulations.

*Year 3.* **Simulations:** Modelling of ice growth through cell membranes and walls – an ambitious goal requiring large-scale molecular dynamics simulations. **Experiments:** Splat assays aimed to assess the morphology of the resulting ice crystals (and their growth kinetics) within bacterial fragments.

Note that at every point in time the unique synergy between experiments and simulations will maximise the impact of the proposed research and allow the student to acquire an exceptional set of transferable skills. The overall goal of the project, that is to understand the origin of “biological” ice in the atmosphere, is an ambitious one that has the potential to lead to important contributions to high-impact factor journals – as demonstrated by the track records of both PI and Co-I.

**Further reading**


Congdon, T., Dean, B.T., Kasperczak-Wright, J., Biggs, C.I., Notman, R., Gibson, M.I., 2015. Probing the Biomimetic Ice Nucleation Inhibition Activity of Poly(vinyl alcohol) and Comparison to
Synthetic and Biological Polymers. Biomacromolecules 16, 2820–2826. https://doi.org/10.1021/acs.biomac.5b00774


Further details

Any enquiries are welcome, especially given the multidisciplinary nature of the project. Please free to contact Dr. Sosso at g.sosso@warwick.ac.uk. Further points of contact can be found at https://www.sossogroup.uk – we are on Twitter as well, @SossoGroup (Dr. Sosso) and @LabGibson (Prof. Gibson).