

## **chameleon: Next Generation Sample Preparation for CryoEM based on Spotiton**

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In the workflow for high-resolution structural determination, improvements in microscope stability, direct detectors and image processing have shifted the bottleneck to sample preparation. The process of obtaining a film of vitreous ice of an appropriate thickness, with evenly distributed particles is not straightforward. Many of the current vitrification methods are highly variable, necessitating the costly step of screening each grid in an electron microscope (EM). Additionally, relatively large sample volumes are required and then lost during the process of blotting, and further grid losses are sustained during the manual handling required to transfer frozen grids into storage, and through poor traceability of storage locations.

The chameleon system is a blot-free, pico-litre dispense instrument for quickly and robustly freezing samples for use in cryoEM. The chameleon system is based on Spotiton [1,2] and uses self-wicking copper nanowire grids to form the thin sample film [3]. This process occurs ‘on-the-fly’ as the grid passes in front of the dispenser on its way to the cryogen bowl, resulting in a stripe of sample across the frozen grid.

This process of grid freezing provides many benefits, including reduced sample requirements and reduced manual handling of grids. Recent publications [4] have demonstrated reduced preferred orientation and aggregation effects in samples that have not been subjected to large wait times while in a thin film. Importantly, the chameleon system also includes an on-board quality control step reducing the time needed to screen and optimize samples. Additionally, the chameleon system includes built-in traceability and reporting.

In short, the chameleon is a sample vitrification system with walk-up usability that also creates opportunities for cutting-edge research despite poorly behaved cryoEM samples.

### References:

- [1] I Razinkov, et al. *Journal of Structural Biology* 195 (2016), p. 190-198
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- [3] H Wei, et al. *Journal of Structural Biology* 202 (2018), p. 170-174
- [4] A Noble, et al. *Nature Methods* 15 (2018), p. 793-795