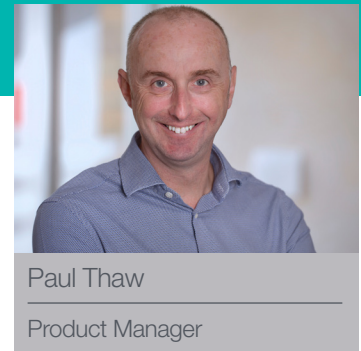


Expert Q&A: Sample preparation for cryo-EM made easier

chameleon - next generation sample preparation for cryo-EM

We spent time with Paul Thaw, Product Manager for Structural Biology, who takes us through where the concept for the chameleon came from, how it differs from what is currently on the market, and the positive impact this unique product will have on researchers' ability to rapidly and efficiently prepare quality frozen grids for Cryogenic Electron Microscopy (cryo-EM).



01 Who did you think would benefit the most when planning this product?

A few years ago, we were lucky enough to visit Richard Henderson's lab at the LMB. They kindly walked us through the workflow from sample to microscope and we could see then that there were several areas where we could potentially improve the outcome for anyone doing hands-on cryo-EM. Having previously been involved in improving automated sample dispensing in X-ray crystallography the grid vitrification process looked like a good fit with our engineering skills and an area where we could make a real difference to the EM community.

02 Where did the original ideas for chameleon come from and what was the process for bringing it to life?

chameleon was actually born out of an academically developed instrument called "Spotiton" which was already actively producing interesting and valuable results for the groups of Bridget Carragher and Clint Potter at NYSBC. It became clear that we had a common interest in providing access to the clear benefits of Spotiton to more structural biology groups. These discussions formed the basis for the ongoing relationship we have to this day. We then set about distilling out what made Spotiton a success and applied our proven engineering and product development knowledge to formulate our own version which we would come to call chameleon.

03 What makes this instrument different to what is currently on the market?

Fundamentally there are four main areas where chameleon differs from existing commercial systems. Firstly, we are using a completely different method for applying the sample to the grid. Instead of pipetting the sample by hand we apply a series of tiny drops using a piezoelectric dispenser to form a stripe on the grid. We've removed the variable paper blotting step and instead use self-wicking grids based on nanowire technology to drive the formation of a thin film ahead of sample vitrification. Secondly, as a consequence of this, we are able to vastly reduce the time between sample dispensing and vitrification to as little as 54 ms compared to the several seconds typically seen on existing plunging devices. Thirdly, a high-speed camera provides instant feedback on likely ice quality, allowing the user to make an informed choice as to which grids should be prioritised for imaging. Finally, ease-of-use improvements like automating nearly all the grid handling steps, improving the ethane condensing process and workflows to walk the user through the process all together act to reduce grid losses and improve the overall condition of the grids when they reach the microscope.

04 What evidence is there that highlights that this new instrument is

A: fit for purpose?

Over the course of its development we've had ongoing visits from over 18 beta user institutions, encompassing more than 80 different samples of varying types. We're beginning to see publications from this work and from some of our early prototype systems. There are some interesting and impactful studies that would not have been possible without the chameleon system – more publications will be coming soon!



B: ready to become an essential instrument for efficient frozen grid preparation?

Thinking broadly, every lab has their share of samples that just didn't work over the years. They perhaps fell apart or were so preferred in their orientations that they couldn't be made to work. With the availability of chameleon, these samples can now be brought out of the freezers and tried again with the current state-of-the-art. For some of them, chameleon may make the key difference that enables their structures to be solved at higher resolutions.

With the ease-of-use improvements and reduced manual handling steps, the chameleon represents a much lower barrier to entry for a scientist new to the cryo-EM field.

I think it's important to say that, as we sit here now, we are in the late development phase of chameleon. We still have some work to do over the coming months and the goal is to transition through to a full manufacturing product as we progress through 2020. We'll continue to work closely with those labs in our early adopter program and beyond to help them generate the results they need. Ultimately it's consistent good results that dictate if any instrument becomes essential in any lab.

05 Is the instrument an intuitive one or does it require lengthy onboarding / implementation?

Much about the chameleon system is different from existing plunge freezing devices on the market. Because of this, there are a number of chameleon-specific concepts that new users are introduced to. We achieve this through independent training materials and on-site training with an Applications Scientist. The chameleon itself walks users through the basic process of grid preparation. Together, this means that users are routinely working with difficult real-world samples during their training and become self-sufficient with helpful support when needed.

06 When is it launching, where can I see one, and when can I place an order?

The system was first shown at the 2019 Microscopy & Microanalysis meeting in Portland. The booth was incredibly busy with visitors, including a launch party with Bridget, Clint and the rest of the NYSBC Spotiton team. Ideally we'd like to do something similar in Europe within 2020. Myself and others in the team have been fortunate enough to be invited to give updates on the chameleon's progress at multiple meetings and it's something we enjoy doing as the cryo-EM community has been welcoming and always provides excellent feedback. In addition to conference talks to share recent results and

new features, we also encourage people to come and see the system in the UK, through demo, or the beta-user program. These visits are invaluable as they allow us to show off the chameleon, but also allow visitors to meet and interact with the broader chameleon team and enable us to understand the evolving needs of the cryo-EM field. We are currently accepting orders for systems and would encourage prospective purchasers to get in touch early due to strong demand for chameleon.

07 What are the biggest impacts that you see for those investing in chameleon?

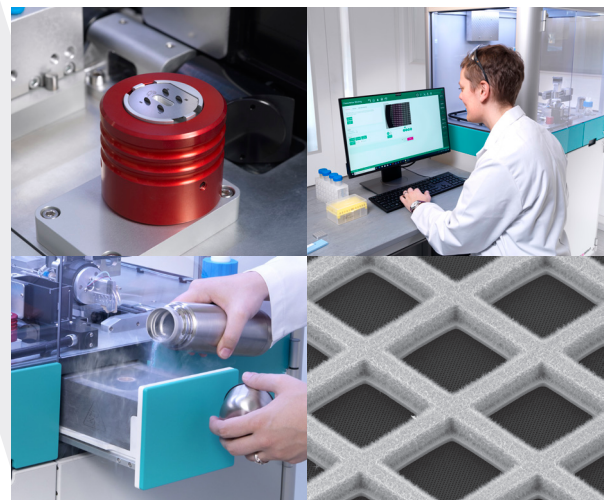
There will be an improvement in the physical condition and overall quality of the grids that go into the microscopes, which will likely equate to a cost savings from putting fewer low-quality grids into an already busy electron microscope. I'm confident we'll also see some gains in data quality and completeness resulting from running at faster plunge speeds for some samples.

08 What are the future plans for the instrument in terms of investment, enhancements and future proofing?

As we near the final design for the current single-particle-focused chameleon, we will begin to focus on what's important to do next. We'll continue to involve the cryo-EM community through in-person discussions, emails and surveys about the kind of features and applications they value most. The chameleon project certainly doesn't stop as we have many exciting ideas to move forward with and tackle next.

09 As the product manager for this product what are you most excited/proud about in relation to chameleon at this stage of its lifecycle?

Actually that's quite an easy question to answer, I would say I'm most proud of all the hard work and commitment that the team as a whole has put in over the years we have been working on chameleon. These things are not easy to achieve, and I've been impressed with the team's willingness to learn and embrace new ideas as well as provide amazing support to the early adopters when needed. They're really committed to delivering something that makes a difference.



Find out about chameleon here:
sptlabtech.com/chameleon