Small molecule electron diffraction may be as old as electron microscopes, but made its popular debut only last year, thanks to teams from PSI [1] and UCLA-Caltech [2]. The new method, called microED, allows researchers to perform crystallographic analysis at the atomic level from simple powders composed of only nanocrystals—and much quicker than ever before. MicroED gives researchers the opportunity to characterize newly synthesized compounds “on the fly,” meaning they can gather important details about a sample throughout its creation, potentially guiding the chemical development process. For the first time ever, a team led by Tim Gruene at the Paul Scherrer Institut was able to show the power of this technique using a commercially-available capsule of a painkiller. Using MicroED, they were able to separate out and characterize one single crystal of the main active ingredient, paracetamol. This technique isn’t just limited to small molecules; peptide samples that were previously considered too unstructured to crystallize can now be analyzed as well [3].

Moving forward, this method, using cryo-EM instrumentation already at our fingertips, will provide structural insight at unparalleled speeds and with higher resolution images. We have created a workflow to make microED fast and easy, and easily accessible to all users. This workflow does also support macromolecular MicroED.