Tim Craggs, Chemistry

Developing a new open-source instrument

The Craggs Lab in the Department of Chemistry have developed a fully open-source instrument for Single-molecule Förster Resonance Energy Transfer (smFRET) measurements, a powerful technique with applications spanning many disciplines across biophysics, biology and biomedicine.

Despite the many advantages of smFRET, which allows scientists to make measurements on a molecule by molecule basis, it is not widely used outside specialist labs. This is largely due to the high costs of commercial instruments and lack of self-build alternatives. To address this, we published a paper in *Nature Communications* [1] including detailed build instructions, parts lists and open-source acquisition software for a new instrument: the smfBox. This would enable a broad range of scientists to perform confocal smFRET experiments on a validated, self-built, robust and economic instrument. The paper has already received more than 6,000 downloads and has generated a large amount of media attention, with coverage by 13 news outlets and an Altmetric score of 220.

Applying open research in biophysics

Through our publication and the linked GitHub site, we provided everything needed to build and run the instrument, from hardware schematics to open-source software. We also provided open-source software for complete analysis of the data, in the form of a series of Jupyter notebooks. This allows other scientists to interact with and modify our datasets, which have a permanent DOI and include both data and analysis. This 'open analysis' approach allows complete transparency in the data we publish. Anyone can reproduce our analysis and figures, or alter analysis parameters to see the effects on the data, thereby establishing for themselves its robustness and any limitations.

As champions of open science and an elected member of the scientific advisory board to the international FRET community, we have encouraged the adoption of a standardised file format - HDF5 - for saving raw data. The HDF5 file architecture is FAIR-compliant, machine-readable and stores all required metadata alongside raw experimental data in a single file. The sfmBox automatically saves metadata and raw data in the HDF5 file format, allowing users to analyse their data with a range of compatible software solutions, including our own open analysis Jupyter notebooks. We are now working with other researchers to help spread the use of this file format.

Open research is not about one thing, it is a way of life in the Craggs Lab, with the overall aim of making our science available, understandable and usable by the largest possible number of people.

Open science is at its best when others can easily take advantage of the progress made, and we have promoted this through video demonstrations of our instrumentation. In the Journal of Visual Experiment, we offer a step-by-step video protocol [2] for using the sfmBox to make accurate single-molecule FRET measurements. To increase access to this article, we have funded the full open access charge from our own consultancy funds (as UKRI pots are ineligible for this – a situation that ought to change).
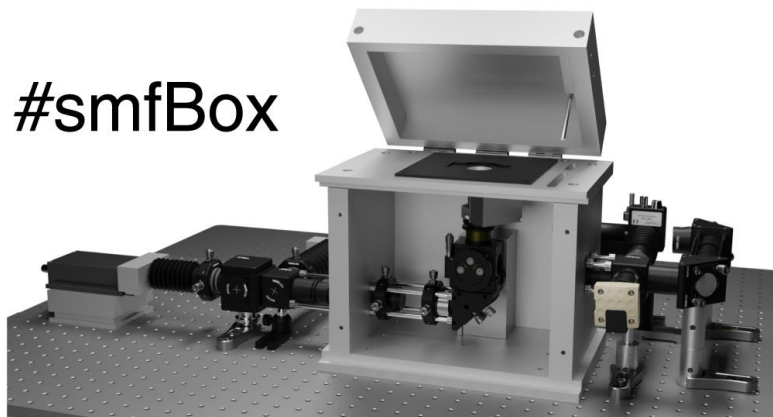
'3D model of the completed smfBox, with the front panel of the microscope body removed' taken from Ambrose, B. et al. (2020)
https://doi.org/10.1038/s41467-020-19468-4 [1]

Looking to the future

Open research is not about one thing, it is a way of life in the Craggs Lab, with the overall aim of making our science available, understandable and usable by the largest possible number of people. As a result of our open research, smfBox is currently being built by at least 5 other labs, in the US, Denmark and South Korea. We are also establishing a spinout company to produce a version of the instrument and software for sale and distribution to labs around the world. This company has received its first pre-seed investment funding, proving that open research can also lead to commercial opportunities.

Our ethos of open research includes many activities, from publishing all of our papers on relevant preprint servers [3] and the new approach of open-hardware instrumentation - in which we have been recognised as early leaders [4] - to establishing open data and analysis through encouraging standardised file formats for our field. Only through this multifaceted approach can open research realise its promise.

Our open research

- Build instructions and parts list for smfBox made openly available
- Open-source software provided in form of Jupyter notebooks
- Step-by-step video protocol made available open access

References

[1] Ambrose, B. et al. (2020). The smfBox is an open-source platform for single-molecule FRET. *Nature Communications* 11: 5641. https://doi.org/10.1038/s41467-020-19468-4
[2] Abdelhamid, M. et al. (2021). Making precise and accurate single-molecule FRET measurements using the open-source smfBox. *JoVE* 173: e62378. https://doi.org/10.3791/62378
[3] Craggs, T. et al. (2018). Substrate conformational dynamics drive structure-specific recognition of gapped DNA by DNA polymerase [Preprint]. *bioRxiv.* https://doi.org/10.1101/263038
[4] Fantner, G. and Oates, A. (2021). Instruments of change for academic tool development. *Nature Physics* 17: 421–424. https://doi.org/10.1038/s41567-021-01221-3