Technology that predicts protein stability is released by UK university spin-out company

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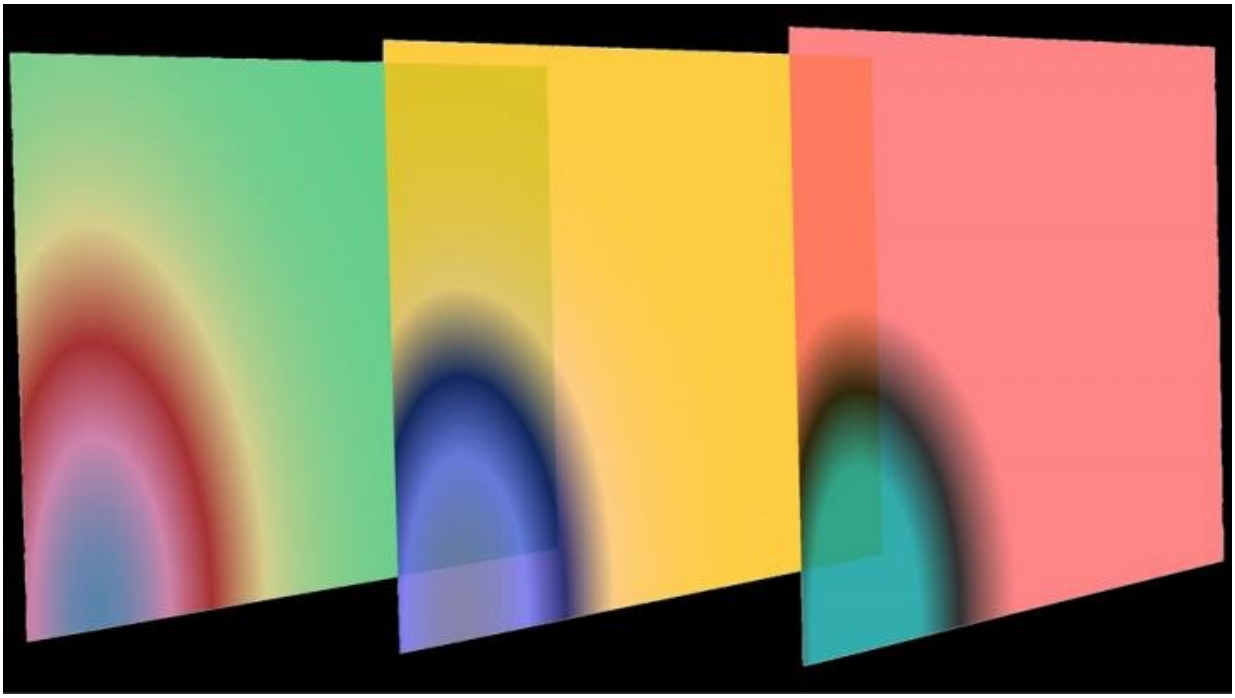

QUBES takes a 'fingerprint' of protein fluorescence and converts it into a prediction of protein stability as well as monitoring for changes in protein structure. QUBES is a cloud-hosted software platform that can be used anywhere with an internet connection. Credit: Chris Pudney, University of Bath

A cutting-edge digital tool that will make it cheaper, safer and faster for pharmaceutical companies to predict protein stability—a vital step in the development of new medicines—is being rolled out by scientists from

the UK's University of Bath through their spin-out company, BLOC Labs.

The tool, launched this week, will help researchers identify the most promising protein molecules for drug development. It has the potential to play an important role in the creation of monoclonal antibodies (mAbs). The market for these therapeutic antibodies is worth over £70 bn.

Monoclonal antibodies are a type of protein derived from natural antibodies and then refined and mass produced in the lab. They are steadily transforming the way we treat and prevent diseases, from cancer and conditions affecting the immune system to viral infections. The coronavirus pandemic has triggered particular interest in mAbs, as a number of protein candidates are showing great promise as therapies to treat COVID-19, and are currently being trialled in humans.

Stability is key

Only mAbs that are known to be stable (that is, they neither break down easily nor clump together to form toxic compounds) are suitable for development, and finding a stable candidate adds massively to the cost and time of finding new drugs.

Until now, the process of determining protein stability has been a big headache for drug companies, with researchers testing vast libraries of molecules in their search for proteins with medicinal properties. However, the tool developed in Bath—called Quantitative Understanding of Bio-molecular Edge-Shift (QUBES) - is able predict the stability of proteins with startling speed and accuracy.

Dr. Chris Pudney from the University's Department of Biology & Biochemistry and developer of QUBES, said: "We're really excited by the potential of QUBES because it can be used immediately in the

biopharmaceutical industry in quality assurance, formulation and development."

He added: "Proteins are notoriously unstable for a good reason—the body wants to recycle them constantly. But with a therapeutic product, you need stability—if a protein breaks down and aggregates, it becomes toxic. Finding stable proteins is hugely expensive for pharmaceutical companies, but using our tool to find the best molecule possible will cut down on the time and cost of development massively."

Qubes fingerprinting

QUBES works by allowing researchers to accurately 'fingerprint' a protein's structure and predict stability under nearly any condition of concentration or formulation. The technique uses fluorescence to map protein structure and then applies a mathematical algorithm, based on the position and type of the protein's atoms, to calculate stability. Thanks to an online suite of software—also developed in Bath—laboratories can interpret their fluorescent data from anywhere in the world, using equipment found in most biochemistry labs without modifications.

Elaborating on the fingerprinting technique, Dr. Pudney said: "Proteins contains tryptophan—an amino acid that emits fluorescent light. Every protein molecule has a unique fluorescent signature, and QUBES leverages this optical phenomenon, applying mathematical techniques to analyse and interpret the fluorescence.

"The software suite takes this academic work and makes it incredibly easy for people to use. You can run it on any machine—even on your mobile phone. It's ultra-rapid and ultra-easy, and it offers an incredibly high level of security—in fact, we have a grade of security that's normally reserved for the financial service industry."

What sets QUBES apart from its competitors is the quality of its readings and its extreme flexibility. Dr. Pudney explains: "Not only is our approach faster, more accurate and more sensitive than anything else on the market, but it can also predict stability at any concentration and in any formulation—unlike other tools on the market, which require set conditions."

Dr. Pudney's team have recently conducted a validation study of the QUBES technology with the National Physical Laboratory (NPL) under the government backed 'Measurement for Recovery Scheme' scheme, which provides independent validation of technology by the country's leading analytical facility.

Dr. Alex Jones, who led the study at NPL, said: "We tested the QUBES approach using a range of analytical methodologies and found that it tracks subtle changes in protein structure and stability with remarkable sensitivity when compared to established methodologies. The approach is fast and simple to implement."

The research is published in the *Biochemical Journal* and the QUBES software is available for commercial trial via BLOC Laboratories Ltd: www.bloclaboratories.com .

More information: Michael J. Knight et al, Monoclonal antibody stability can be usefully monitored using the excitation-energy-dependent fluorescence edge-shift, *Biochemical Journal* (2020). DOI: 10.1042/BCJ20200580

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