Abstractions

LAST AUTHOR

Mass spectrometry is a valuable tool for identifying and characterizing biomolecules, but the technology has limitations. Gary Siuzdak, director of the mass spectrometry centre at the Scripps Research Institute in La Jolla, California, and his colleagues set out to improve the technique's sensitivity and ease of use for analysing metabolites, single cells, biofluids and tissues. On page 1033 they describe how combining a nanostructure with chemical initiators made this possible.

What fuelled this work?

Mass spectrometry is commonly thought of as a mature technology, but it has constraints, including the breadth of molecules that can be analysed and its ability to separate molecules in a complex mixture. Our primary motivation was to move it forward.

Why use nanostructures to alter how the ions are generated?

To measure a molecule's characteristics using mass spectrometry, a gas-phase ion of that molecule has to be generated. My co-author Trent Northen wanted to develop a technique for more efficient ionization. We designed a silicon surface with nanometre-sized pores that can trap highly fluorinated initiator molecules (known as clathrates) that can be used to coat the molecule of interest. When the nanostructure is heated with pulsed laser irradiation, it efficiently vaporizes the molecule along with the initiatior, which ionizes the molecule.

What types of sample did you test first?

We focused on metabolites — small molecules generated during metabolism — as these have proved useful as biomarkers of disease. The most readily available were in our own biofluids, namely urine.

What applications do you find most interesting?

Metabolomics, the study of metabolites found in blood and urine, as well as the ability to profile single cells, are both of great interest to us. Because our approach involves minimal sample preparation, we believe it could lead to clinical applications. We also show that it can effectively image tissues — we use it to reveal the complex ionic profiles of developing tissue types in thin slices of mouse embryo.

What impact might this method have for biology?

This is a simple, high-throughput, robust and sensitive technology that will find uses in everything from determining the composition of microbial communities to profiling the structure of stem cells. To make the technology accessible to a wide audience, we've created a video guide. ■

MAKING THE PAPER

Claudio Stern

Technology reveals the movements of single cells in early development.

After more than 30 years studying embryo development, Claudio Stern has finally realized his dream: to see exactly how cells behave during one of the earliest periods of embryo formation. Technology allowing the viewing of individual cells within an intact organism has only recently become available, and Stern, a developmental biologist at University College London, was eager to try it out.

Gastrulation is a period in early embryonic development during which massive cell migration leads one layer of cells to develop into three. These will go on to form different organs. Chick embryos — Stern's chosen animal model — begin this process as a flat disc of cells. A crease called the primitive streak forms across the disc and acts as a passageway, through which cells flow inside the embryo, forming two new layers.

Stern first began working as an embryologist in the 1970s, when he was a graduate student in Brian Goodwin's lab at Sussex University, UK. Goodwin offered him an array of projects: salamander limb regeneration, slime-mould migration, moth wing patterning, regeneration in the unicellular plant Acetabularia and "the chick."

"I asked him, 'What about the chick?' and he said, 'Anything you like'," recalls Stern, who chose to study gastrulation. Goodwin gave him a Second World War 16-millimetre Vinten cine camera to use for time-lapse filming.

This had been done before. German anatomist Ludwig Gräper was among the first to study cell movements during gastrulation in living chick embryos. In 1926, he made three-dimensional time-lapse movies of embryos. Although Gräper couldn't see individual cells, he could see their global movements, especially the shuffling of the cells as they made their way to the embryo's centre to create the primitive streak. He dubbed these 'Polonaise movements', after a popular dance in which dancers move along opposite sides of the room before turning inwards at the end, whereupon they meet and form pairs, then move down the centre of the room.

"It has taken more than 80 years to see details of the cells during these movements," says Stern. His group now uses the recently developed multi-photon microscope, which can penetrate deep into tissues and obtain high-resolution three-dimensional images. Because the chick embryo is fairly transluscent and flat, imaging is easier than in organisms such as the mouse, whose cup-shaped embryo and maternal tissues obscure the view.

To see the movements of individual cells, postdoctoral fellow Octavian Voiculescu used single lines to connect groups of three cells into triangles on each video frame. He then compared the movement of triangles in different regions of the embryo. From this, he discovered that embryonic epithelial cells push in between their neighbours — similarly to the Polonaise dancers who pair up as they weave into the middle of the room — before the primitive streak starts to form (see page 1049 and http://tinyurl.com/275aur).

"At low power, the movements look organized. At high power, it looks like rush hour, with people fighting for a door," says Stern. "It is only by looking at the relationships between cells — the triangles — that the order becomes apparent."

The team also showed that a major signalling pathway, known as the Wnt planar-cell-polarity pathway, guides these movements. The group now hopes to analyse cell movements from the side, perpendicular to this current view, to try to reveal how these movements are possible, given that the cells are held rigidly together by tight junctions. ■

FROM THE BLOGOSPHERE

Juan-Carlos Lopez, Editor of *Nature Medicine*, writes on 'Spoonful of medicine' (http://tinyurl.com/25e2o2): "Checking the literature in preparation for our monthly News & Views meeting, my colleague Clare Thomas spotted this recent paper from *PLoS Pathogens* [X. Contreras *et al. PLoS Pathog.* **3,** e146; 2007]: HMBA Releases P-TEFb from HEXIM1 and 7SK snRNA via PI3K/Akt and Activates HIV Transcription. No offense intended to the authors or the editors, but I think it's safe to say that there's one too many abbreviations in the title. Can anyone out there trump it?"

Meanwhile, there is plenty of writing advice online. The *Nature Nanotechnology* 'Asia Pacific and Beyond' forum on Nature Network features a tips column for technical writing (http://tinyurl.com/2kvdhu). Here, for example, the sentence "The design of the microscope incorporates aberration lenses, 3 different lasers, which are suspended above the lenses which is housed in a chamber" is simplified by associate editor Ai Lin Chun to "The microscope consists of aberration lenses and three different lasers. Each laser is suspended above the lens and housed in a chamber." ■

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