

One in a Million

By [Jason Socrates Bardi](#)

"Our main tool of choice is flow cytometry," says Associate Professor Michael McHeyzer-Williams. This tool allows him to analyze components of the immune system and immunological processes one cell at a time.

Flow cytometry was invented early 1970s by a group at Stanford led by Len Herzenberg, who patented his "fluorescence activated cell sorter" in 1972. The technology was similar to a device used by geologists to interrogate samples of stone to determine mineral composition. The technology arose after scientists had found a way to generate antibody-containing reagents that are specific for particular proteins or other individual markers on the surface of cells. What Herzenberg did was to attach fluorophores—colors—to these antibodies.

Analytically, the actual detection is based on the fluorescence of the fluorophores to which antibodies have been attached. Different antibodies have different fluorophores, which give different colors. In a typical flow experiment, some tissue or organ is dissociated into single-cell suspensions and labeled with the colored antibodies. The more colors you use, the more separating power you have.

When McHeyzer-Williams was in graduate school, for instance, he worked with four different antibodies and four different colors to sort his cells based on four different surface molecules.

Through the years, the technique has developed



Associate Professor Michael McHeyzer-Williams and the flow machine. Photo by Michael Balderas.

incrementally into a powerful tool for everything from the high speed sorting of cells by cell type to the isolation of a single cell from within a large population of cells.

Flow cytometry is also now much faster than it used to be. Instruments typically can sort through 6,000 cells per second and the fastest ones can sort through 25,000 per second. But the number of colors that can be used has also improved, and with it, resolution.

"Every time you add a color, you increase the resolution of the sub-population of cells you can find by 10-fold," says McHeyzer-Williams. He himself uses six colors routinely, which allows him to find one cell in 100,000 or one in a million.

The power of flow is not derived solely from the technology, the instrument, but also from the biology—the nuanced strategy that a scientist like McHeyzer-Williams employs to identify the right population of cells. There is a lot of strategy involving variables such as how to run the experiment and which colors and antibodies to use.

Flow cytometry is a powerful way of looking for the proverbial needle in a haystack. More descriptively, it is a way of taking a haystack, running it down a conveyor belt one straw at a time, and finding the needles because they are shinier than everything else.

In the apparatus, the cells in a buffered solution stream through a small tube in the instrument, and they flow past a detector built with one or more lasers (McHeyzer-Williams's brand new instrument has three). The lasers blast the flowing cells with light at particular wavelengths, and various wavelengths excite the various fluorophores if they are present on the surface of the cells. A lens and an optical bench full of charged coupled devices like those you might find in a digital camera resolve the different colors of emission, and a computer combines these into a picture.

Flow cytometry can be used in tandem with other

techniques and technologies like quantitative PCR or gene microarrays, which then allow you to sort the cell and then ask what genes are being expressed therein or how much of one particular gene is being expressed.

So to further the analogy, flow cytometry is like a way of finding a needle in a haystack where once you find it, you can also ask where that needle came from, when it was made, and who made it.

"Flow is not just the instrument," says McHeyzer-Williams. "It's the way you design [the experiment]."

[Go back to News & Views Index](#)