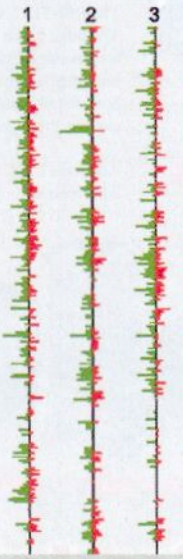
Caryoscope: Putting Microarray Data in Chromosomal Context

Software correlates expression patterns with location

Microarrays are wonderful tools for seeing global patterns of gene expression under different conditions. Plenty of software exists to make sense of the data, but what if you want to correlate expression patterns with location? Perhaps Caryoscope can help.

Rather than forcing users to stare at endless columns of data or the traditional Rorschach-like microarray readout, Caryoscope (caryoscope.stanford.edu) overlays color-coded microarray data onto a chromosomal map. "It allows you to view gene-expression data within the context of the genomic structure," says Gavin Sherlock, the Stanford University geneticist who oversaw Ihab Awad, the program's primary author.

Researchers can download Caryoscope (a component of the Generic Model Organism Database project) as a Java applet (current version 0.3.9) for local use, or run it remotely on Stanford's servers. Accepted file formats include tab-delimited, comma-delimited, and GFF (general file format, an emerging standard for microarray data), all of which can be generated by the Stanford Microarray Database (SMD).



Each data point can have associated pop-up text and hyperlinks to provide additional information (e.g., the URL could redirect the user to gene-specific information). And the program isn't limited to expression data; other numerical data can be graphed, too, as long as it can be associated with chromosome location information.

The program fosters remote collaboration by providing password-based access. But Sherlock, who helps to oversee the SMD, hopes to see it make raw published data more readily available. "This is a step towards openness in the genetics community," he says.

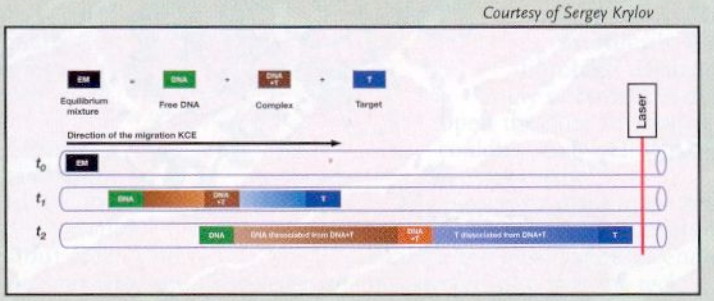
—Sam Jaffe

Toward a Diagnostic "Swiss Army Knife"

Canadian team develops tool to probe protein content of individual cells

Researchers at York University in Toronto are refining a new bioanalytical technique capable of simultaneously analyzing hundreds or thousands of proteins in individual human cells. Sergey Krylov, Canada Research Chair in Bioanalytical Chemistry at the university, and his colleagues say they hope that kinetic capillary electrophoresis (KCE) will allow them to create what they've dubbed a diagnostic "Swiss Army Knife," eventually able to diagnose and treat diseases such as cancer, Parkinson, and Alzheimer. "It is very new, very sexy. We are integrating KCE with chemical cytometry, directly and indirectly," says Krylov.

Courtesy of Sergey Krylov



Indirectly, Krylov uses the technique to select and characterize aptamers, which are DNA molecules that can fold to bind a protein or other analyte. Aptamers have both pure research and pharmaceutical applications. First, a randomized DNA library is mixed with the target and subjected to capillary electrophoresis. As the run proceeds, the mixture resolves into free DNA, DNA-target complex, and free target. Krylov collects the DNA-target complexes and then repeats the cycle until a suitable high-affinity molecule is obtained. His group found that the approach exceeds traditional selection methods by two orders of magnitude, producing an aptamer that can bind a protein such as farnesyltransferase with nanomolar affinity in one round.[1]

Other applications, or "blades," include aptamer characterization and target quantification (in this case, the amount of farnesyltransferase present in a given cell). Krylov says his group also has developed a two-channel chemical cytometry method to probe sister cells simultaneously; he is using the technique to study stem cells, hoping to learn how to control their division and differentiation. Such findings could, in turn, lead to techniques for tissue regeneration.[2]

Andy Ellington, an aptamer expert of the University of Texas who has worked with Krylov on nucleic acid separations, writes via E-mail that the developments in chemical cytometry will have a "major impact" in its ability "to identify patterns of chemical differences between single cells." He explains: "In general, measurements are carried out on populations of cells. While techniques such as FACS [fluorescence activated cell sorting] can observe single cells, it is difficult to coordinate perturbing cellular metabolism with the identification of how individual cells are affected by such perturbations. The methods developed by Dr. Krylov and his coworkers overcome this problem, in that each cell is now subject both to manipulation and observation."

—Doug Payne

References

1. M. Berezovski et al., "Nonequilibrium capillary electrophoresis of equilibrium mixtures (NECEEM)—a "Swiss army knife" for selection of aptamers," submitted to *Proc Natl Acad Sci*, Aug. 23, 2004.
2. K. Hu et al., "Asymmetry between sister cells in a cancer cell line revealed by chemical cytometry," *Anal Chem*, 76:3864–6, July 1, 2004.