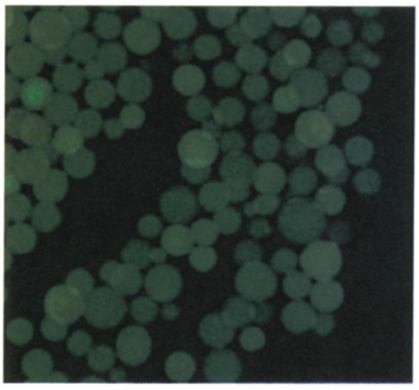
Bind and shine

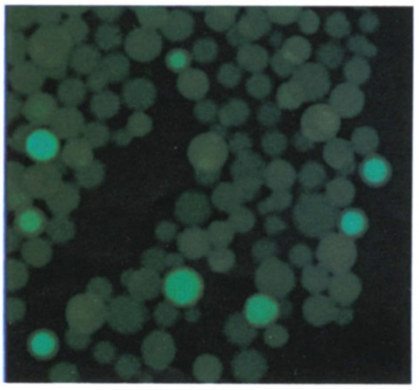
Synthetic chemosensors could play a large role in future analysis of biological systems, finding uses as *in vitro* library screening tools or as a means to detect peptide release *in vivo*. A recent paper describes an advance in chemosensor technology: the synthesis of a pair of small organic sensor molecules that bind to different tripeptides in a sequence specific manner and fluoresce dramatically when bound (Chen, C.-T., Wagner, H. & Still, W.C. *Science* **279**, 851–853, 1998). These small molecules consist of a fluorescence energy transfer system made up of a fluorophore and a quencher. When a peptide binds, it prevents quenching.

The peptide-binding portion of these chemosensors consists of known sequence selective amide-linked oligomers of isophthalic acid and cyclic *trans*-1,2-diamine derivatives. These bind specifically and with high affinity because they are conformationally restricted and have a concave binding site with nearby hydrogen bond donors and acceptors. Chen *et al.* synthesized two molecules of this type and then determined their peptide specificities by screening a combinatorial tripeptide library immobilized on polystyrene beads, with one type of sequence per bead. Those beads that bound the chemosensor were easy to identify in this case because of the natural orange color of the chemosensor. The peptides coupled to the selected beads were sequenced, and experiments to measure affinities were performed. One of the chemosensors bound (D)Pro(L)Val(L)Gln with a low μM K_d, and control experiments showed that diastereomeric changes had large negative effects on binding: (L)Pro(L)Val(D)Gln bound tenfold less well and (D)Pro(D)Val(D)Gln did not bind at all. Significantly, when bound to their cognate peptides, the chemosensors showed dramatic increases of 100–500% in their fluorescence.

In most biological cases, the target peptide will be known and the goal will be to find a suitable chemosensor, and thus the screen described above would have to be reversed, using a library of synthetic chemosensors instead of peptides. Toward this end, Chen *et al.* coupled a characterized sequence-specific chemosensor to polystyrene beads. When the cognate peptide solution was added, the chemosensor-coated beads glowed quite visibly through a fluorescence microscope. No cross reaction was seen with different peptides, suggesting that libraries of potential chemosensors coupled to beads could, in fact, be screened for peptide binding in this manner. The figures show a pilot screening experiment with a small number of beads, each bound to a different type of synthetic chemosensor. After the solution containing one type of tripeptide was added, a number of beads (presumably each with a chemensor that recognizes the peptide) glowed brightly and could be readily separated from the others for further analyses.



Before peptide addition



After addition of peptide (Ac D-Pro L-Val D-Gln)

Of course, making these synthetic organic molecules user friendly for biologists may not be so easy. The caveat is that this work was done in $CHCl_3$. Hopefully — if this technology is to be useful in biological systems — it can be extended to water based solutions. TLS

Who was Ångström?

Anders Jonas Ångström was born in Sweden in 1814. At the age of 25, he was already a lecturer at his *alma mater*, the University of Uppsala, Sweden, in the physics department, and he later became the chair. Ångström was a pioneer in spectral analysis, a field that began when Isaac Newton demonstrated, using a prism, that white light is made up of numerous colors. Among his accomplishments, Ångström initiated studies on the spectrum of hydrogen, and later followed up on the work of three contemporaries — Joseph von Fraunhofer, Gustav Robert Kirchhoff and Robert Wilhelm Bunsen — who began to measure the many dark lines that interrupt the solar spectrum. These lines (now known as Fraunhofer lines) are caused by selective absorption (at specific wavelengths) of the Sun's radiation by elements in its atmosphere. Ångström measured Fraunhofer lines in the solar spectrum, introducing a convenient unit, 10^{-10} meter, for describing wavelengths in absolute terms. His work produced the most complete map of the solar spectrum for his time. Ångström also investigated a mystery that had puzzled those in the far north for centuries; he analyzed the spectrum of the *Aurora Borealis*, the Northern Lights, showing that it differed from that of the Sun and thus refuting the idea that auroral light was reflected sunlight. Ångström died in 1874, but it was not until 1905 that the unit of 10^{-10} meter — an obviously useful unit since it is the typical diameter of an atom — was named after him. TLS