Using Multilayer Soft Lithography Formulator Chips to map Precipitations Diagrams of Proteins

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In the post human genome era, the focus has shifted from sequencing genomes to investigate the proteins that are encoded by the genomes. The structural genomics programs have different missions but they all share the fact, that they have put together a high throughput pipeline that make it cheaper, easier and faster to get from gene to the three dimensional structure of the encoded protein. In this pipeline there are several bottlenecks, but it is agreed in general that the most significant bottleneck is to get from the protein solution to protein crystals of diffraction quality.

We have implemented the method of Multilayer Soft Lithography to produce Formulator chips [1] to address the problem of protein crystallization. Using the Formulator chip, the solubility behaviour of a protein can be experimental characterised using minute volumes of sample. The protein is screened against 3000 chemical conditions using less than 10 µL of purified protein sample. Subsequently 30 to 50 chemical conditions from this sparse screen are selected for detailed mapping of the precipitation diagram, in which the concentrations of protein against precipitant are varied. Using the experimental precipitation diagrams tailor made crystallisations experiments are designed, maximizing the probability of producing crystals of the protein.

[1] Hansen C.L., Sommer M.O.A., Quake S.R., *PNAS USA*, 2004, **101**, p14431-14436.

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