The Nanopore Mass Spectrometer

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We are developing a technique to sequence proteins at the single molecule level. Our approach merges the ability of nanopores to force polymers to translocate in a linear fashion with the ability of mass spectrometry to identify individual amino acids. The nanopore in our setup takes the form of a capillary that has been pulled into a needle-like tip with an opening on the 10 - 100 nm scale. Amino acids are drawn out of solution and into the mass spectrometer by the application of strong electric fields through a process known as electrospray ionization. A single molecule approach could drastically increase the speed and reduce the cost of protein sequencing, which remains slow and expensive, especially in comparison with DNA sequencing. It would also alleviate the usual requirements for large samples and allow for the possibility of collecting sample from a single cell and measuring relative protein abundances.

My research is focused on establishing sets of conditions that will allow us to identify all 20 amino acids. Amino acids are challenging to identify due to their wide range of iso-electric points (IEP). Depending on the pH of the solution, they can be positive, negative, or neutral. And, in order for amino acids to be identified in our mass spectrometer, they must be charged. Our results demonstrate that we can detect both positive and negative ions of amino-acids. So far we have observed stronger signals from positively charged amino acids. Generally in the positive-ion mode, electrospray ionization mass spectrometry (ESI-MS) results in protonated molecules, $[M+H]^+$. However, for some molecules the formation of alkali metal ion adducts, like $[M+Na]^+$ or $[M+K]^+$, instead of proton addition are often observed. When the process is not controlled, facile adduct formation can lead to large variations and unreliable results. We have been able to avoid alkali metal ion adduct formations, and we can easily discriminate the alkali ions from the amino-acids when they are mixed in solution. Interestingly, our mass spectra of amino-acids do not reveal any formation of alkali metal ion adducts (e.g. $[M+Na]^+$ or $[M+K]^+$), which are common features in conventional electrospray ionization mass spectra. The absence of those peaks makes our spectra easier to interpret.

We designed a setup that allows us to exchange solutions while our experiment is running. This setup allows us to change the concentration of the solution or to analyze several compounds with the same nanocapillary. It also allows us to rapidly modify conditions (pH, salt concentrations, amino-acids, …), and compare the results with a reference sample studied in the same conditions.