In-Capillary sample concentration in CE – "This is my analyte, how do I stack?"

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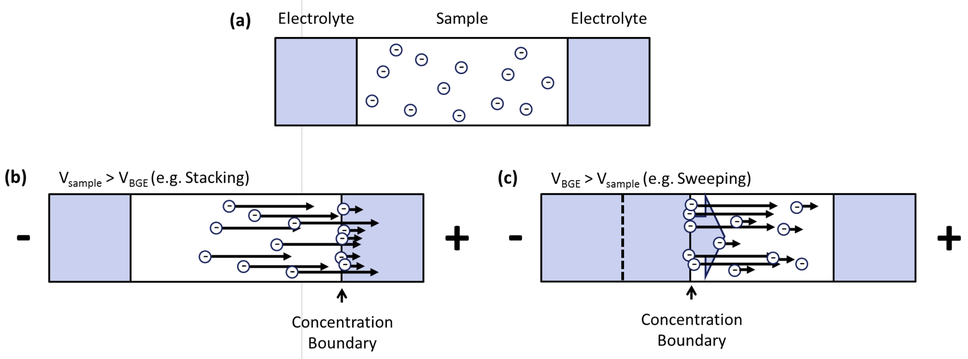
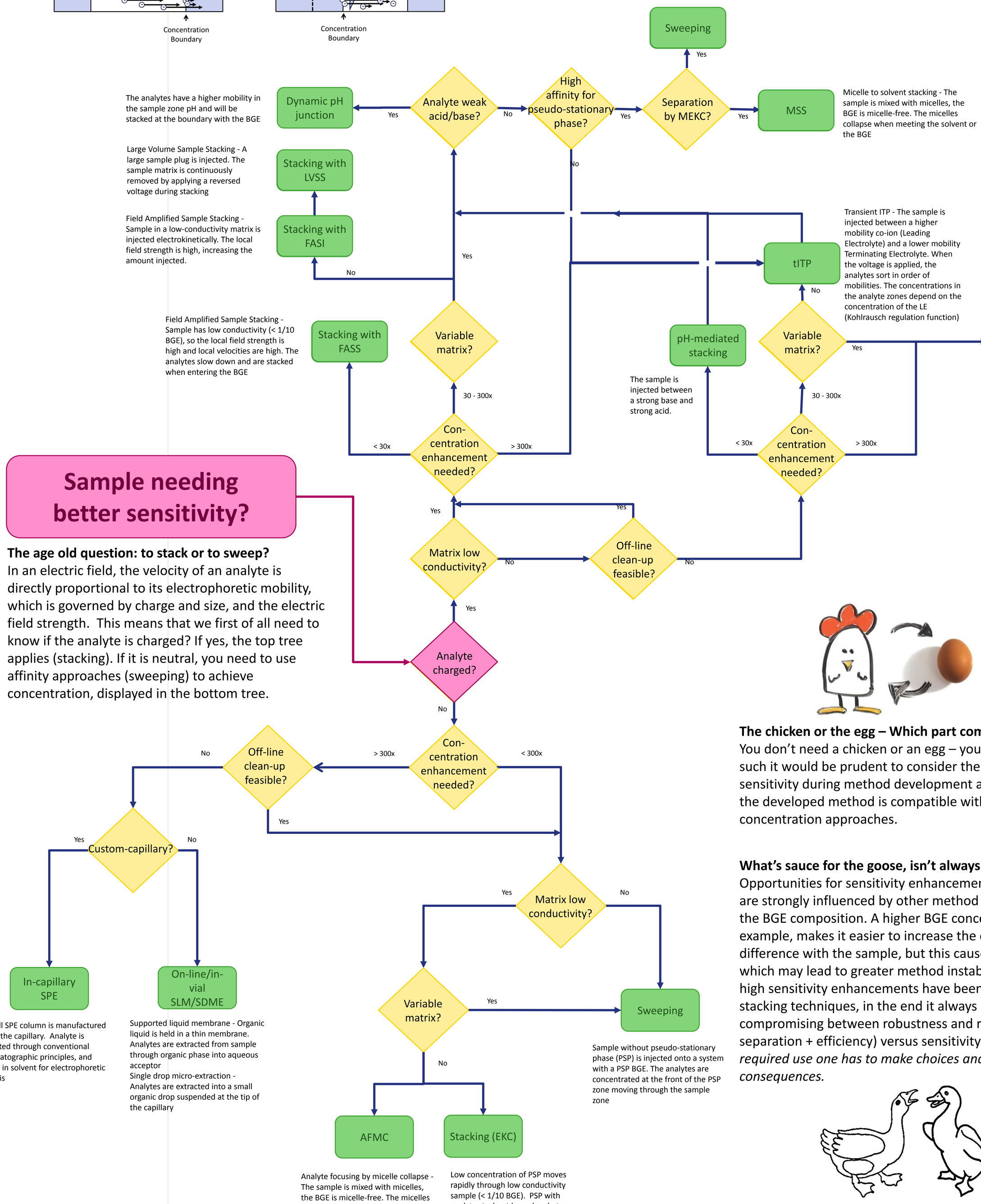
All concentration methods in CE involve creating a velocity difference between the sample and the BGE. The challenge is how this can be done.



Usually, reviews discuss all different techniques from the mechanistic point of view. Here, we'd like to turn it around and ask the question:
I have XYZ in my sample, how do I improve my sensitivity?

Concentrating in CE - Creating velocity differences of the analyte in the sample zone vs. the velocity of the analyte in the BGE



Sample needing better sensitivity?

The age old question: to stack or to sweep?
In an electric field, the velocity of an analyte is directly proportional to its electrophoretic mobility, which is governed by charge and size, and the electric field strength. This means that we first of all need to know if the analyte is charged? If yes, the top tree applies (stacking). If it is neutral, you need to use affinity approaches (sweeping) to achieve concentration, displayed in the bottom tree.

A small SPE column is manufactured inside the capillary. Analyte is extracted through conventional chromatographic principles, and eluted in solvent for electrophoretic analysis

Supported liquid membrane - Organic liquid is held in a thin membrane. Analytes are extracted from sample through organic phase into aqueous acceptor
Single drop micro-extraction - Analytes are extracted into a small organic drop suspended at the tip of the capillary

Analyte focusing by micelle collapse - The sample is mixed with micelles, the BGE is micelle-free. The micelles collapse when meeting the solvent or the BGE

Low concentration of PSP moves rapidly through low conductivity sample (< 1/10 BGE). PSP with analyte stacks at boundary between sample and electrolyte

Sample without pseudo-stationary phase (PSP) is injected onto a system with a PSP BGE. The analytes are concentrated at the front of the PSP zone moving through the sample zone

The chicken or the egg – Which part comes first?
You don't need a chicken or an egg – you need both. As such it would be prudent to consider the requirements of sensitivity during method development and to ensure that the developed method is compatible with some of the concentration approaches.

What's sauce for the goose, isn't always sauce for the gander
Opportunities for sensitivity enhancement through injection are strongly influenced by other method parameters, such as the BGE composition. A higher BGE concentration, for example, makes it easier to increase the conductivity difference with the sample, but this causes higher currents, which may lead to greater method instability. Although very high sensitivity enhancements have been published with stacking techniques, in the end it always comes to compromising between robustness and resolution (= separation + efficiency) versus sensitivity. *Depending on the required use one has to make choices and take the consequences.*