Differential Ion Mobility Separations in Pure Helium and He Mixtures Using Microchips

Alexandre A. Shvartsburg, Yehia Ibrahim, Richard D. Smith
Biological Sciences Division, Pacific Northwest National Laboratory

Overview
- FAIMS microchips extremely resistant to electrophoretic interferences. Permit separation in 100% He and all He mixtures with any gas
- We explored the dependences of FAIMS separation parameter (compensation field, $E_C$, resolution, and resolution/sensitivity) on ion mobilities and parameters on the He fraction in He/Ne buffers across the full composition range
- Evaluation involved Owston chips of generations I (35 um gap) and current II (100 um gap).
- Evolution of $E_C$ values between N$_2$ and He can be rationalized from first principles, showing the path to a priori physical theory for FAIMS separations

Methods
- **Fundamental premise**
  - Evolution of separation parameter: $f_{E_C}$ for any gas goes up with increasing gap width ($w$).
  - For $N_2, f_{E_C} = 0.27$ at $w = 0.35$ mm, at $0.25$ mm [4].
  - Hence FAIMS chips with multichannel gap ($60 \times 0.35$ mm) can use much higher dispersion field ($E_C$) than ‘full-size’ devices ($w \geq 0.35$ mm) limited by the waveform generator (is ~35% of $E_C$).
- **Implementation**
  - Microchips were Owston Ltd, Cambridge, UK (etched with 50% open surface) aluminum nitride, wire gauze vapor deposition, packaged, and mounted on a printed circuit board [4].

Results
- **Resolving power and resolution for peptides**
- Mass-scaled FAIMS using ‘wedge’ gaps.
- Adding He to the buffer (typically nitrogen) to maximize $E_C$ to 100% He, but at $w = 0.05$ mm (limited by the waveform generator) is just ~35% of $E_C$.
- Therefore microchips should allow high He fractions.

- **Metabolite analyses**
  - A major emerging FAIMS application is metabolomics. Most metabolite ions generated by ESI are singly charged. We looked at the separation of neuropeptide (893 Da) and lipids [18:1/18:0/16:0 (TAG), 895 Da] for $E_C = 0.00$ to 1.4 mm.
  - Resolution/sensitivity balance at 80% He
  - Effects of He similar to but weaker than those for full-size devices: more energetic collisions shift all gas molecules closer to hard spheres.
  - Successor 1.4 mm $E_C$ for ions in N$_2$ and He is encouraging for the development of predictive model for FAIMS separations using helium.
- Pure and mixed H$_2$ buffers should also work

Conclusions
- **In line with theory** [8], E$_C$ for many species maxima ~80% He, effects of He weaker than for full-size FAIMS devices.
- Most resolution/sensitivity balance at 80% He.
- **Patterns for full-size devices**
- Most narrow peaks, improves resolution; but the difference between E$_C$ in N$_2$ and He is encouraging for the construction of a model FAIMS theory for the construction of predictive models for FAIMS separations using helium.

Introduction
- **Differential or Field Asymmetric waveform IMS (FAIMS) separations depend on the buffer gas composition more strongly than on the sheath gas composition** (conventional IMS). As the nonlinearity of FAIMS magnifies small effects of specific ion-mobility interactions on ion mobility [4].
- **Addition of helium to the buffer (typically nitrogen) broadly raises FAIMS resolution because of**:
  - 1. **Lighter ions** (e.g., lighter gases, helium) and the control module
  - 2. **Resolution power scales as $K^2\times w$ and the control module**
- **Non-linear effect**
  - He addition to the buffer gas mixture decreases from weighted averages between $K$ values in pure components. This tends to increase $E_C$ and thus the resolving power [1].

Electrical boundary limits ‘full-size’ FAIMS devices: maximum waveform amplitude (displacement voltage) to 70% of $E_C$ for N$_2$, has become the buffer of choice.

- **Mobilities measured by linear IMS can be related to ion geometries by matching to computed values** [3]. That has not been achieved for FAIMS because high-field ion mobilities are much harder to model. Simplest ionic-molecular interactions are for He, which has intermediate IMS data and so do for FAIMS.

- **Hence enabling FAIMS in helium is desired for both fundamental and analytical reasons**.

**References**

**Contact:** Dr. Alexandre A. Shvartsburg, alexandre.shvartsburg@pnnl.gov

**Career Opportunities**
For potential openings with the Omics Separations and Mass Spectrometry Group at PNNL, write to: Dick Smith at ds@pnnl.gov; Josh Adkins at joshua.adkins@pnnl.gov

**www.omics.pnl.gov**