

Research in the Bleiholder Group: Ion Mobility-Mass Spectrometry



- Shown here is the Bleiholder lab's TIMS-QTof in its current configuration.
- Coming soon a two meter long drift tube will be also interfaced to this instrument.



- lons are produced at a source and deflected into an entrance funnel. They are focused radially by an RF field, and driven axially by a DC field and flow of buffer gas. • Upon entrance to the analyzer region lons are held stationary by the flow of buffer gas going towards the exit funnel and an electric field gradient going in the opposite direction

• Heart disease and cancer metastases are the leading cause

- Chemokines are a family of small proteins that regulate where
- The molecular mechanism of how chemokines regulate cell
 - Chemokine functions depends on the distribution of co-existing conformations and oligomeric states.
 - We use IM-MS to trap distinct conformations of chemokines and their assemblies.

3. Results

cause of heart disease).



modulates the structural diversity of dimers as well as monomers, suggesting the mechanism of allosteric control of CCL5 oligomerization by I-S.

Electric Field Gradient

- The 14 cm ion mobility portion of the instrument consist of a deflector, entrance funnel, analyzer region, and two more smaller downstream funnels.
- The mobility separation takes place in the 4.7 cm long analyzer region
- In the analyzer a flow of buffer gas pushes ions against an electric field towards the exit funnel. lons are trapped separated according to their mobility.



• lons come to rest in the analyzer and elute where $F_{electric} = F_{friction}$ $(F_e = F_f)$. Larger ions penetrate further into the field than smaller ions due difference in frictional force.



One major goal of our group is to improve IM-MS technology for use in structural biology (Jointly with Bruker Daltonics).

Motivation

High throughput structural analysis requires a fast algorithm method that can accurately approximate the Collision Cross Section (CCS) of molecules for a variety of buffer gases' polarity and with a variety molecular charge distributions (MCD). Evaluation of the accuracy and the reliability of the current PSA method is pursued here.

Problem



5. Method Development

Shown are multiple conformations of the ubiquitin 7+ charge state, with conformational dependence on RF. If Instrument parameters aren't carefully chosen observed conformations won't reflect the solution phase.

