

Outline

- Computational models for real life microfluidics applications developed at Corning IntelliSense.
- Typical applications
 - Capillary electrophoresis based devices (proteomics, other chip based separation)
 - Zone Electrophoresis
 - Iso-electric focusing
 - Isotachopheresis
 - BioMEMS array devices
 - Flow sensors and controllers
 - Generic flow and heat transfer devices

Computational Modeling of Microfluidics Applications

Challenges of MF Applications

- Transport phenomena involving multiple driving forces that are coupled.
- Complex geometries.
- Multi-physics with disparate spatial and temporal scales.
- Presence of chemically active analytes.
- Special boundary conditions.

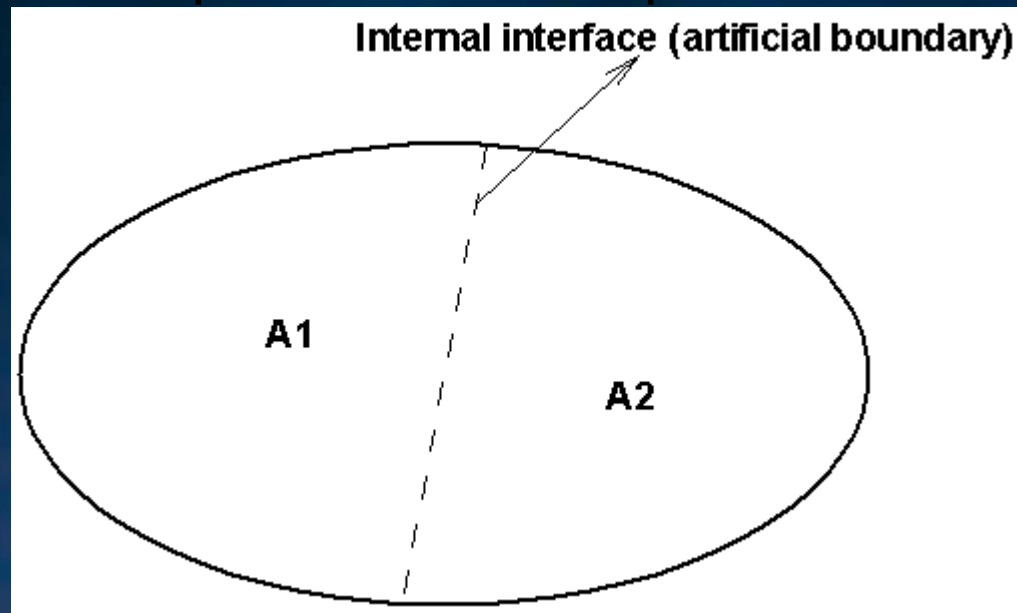
Computational Modeling of Microfluidics Applications

Strategy

- Generalized, scalable formulation to account for multiple driving forces.
- Accurate modeling of geometry – meshing.
- Formulation to handle coupling of various physical phenomena with transport phenomena.
- Computationally efficient and scalable formulation.
- Multi-scale formalism.

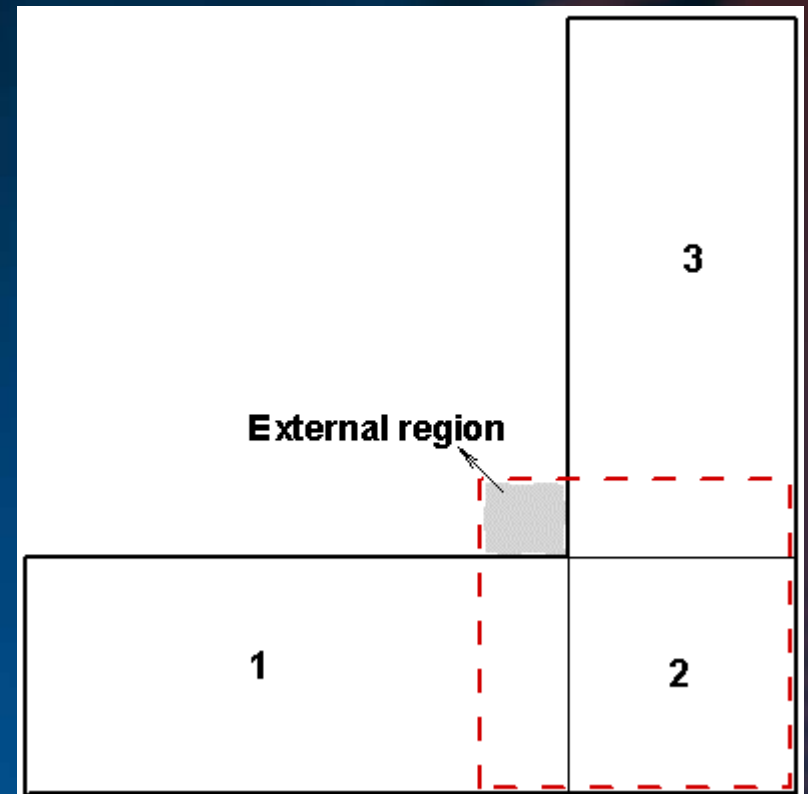
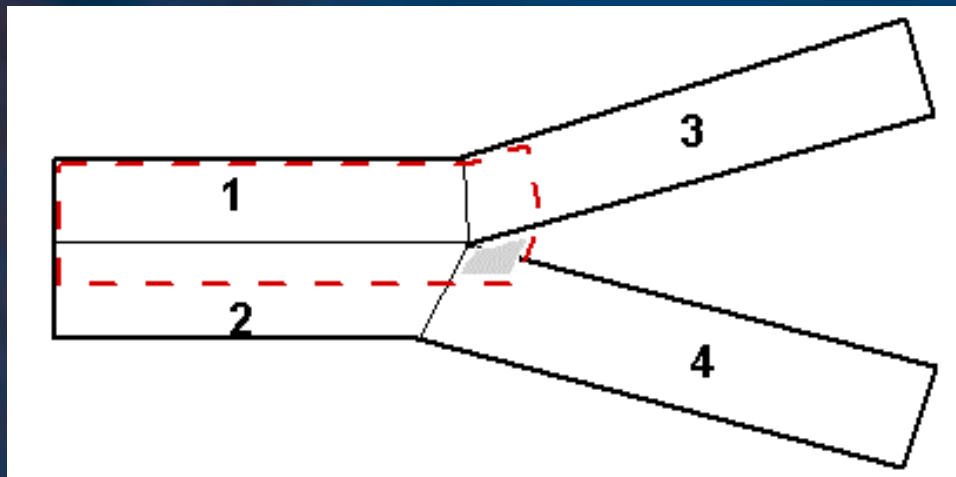
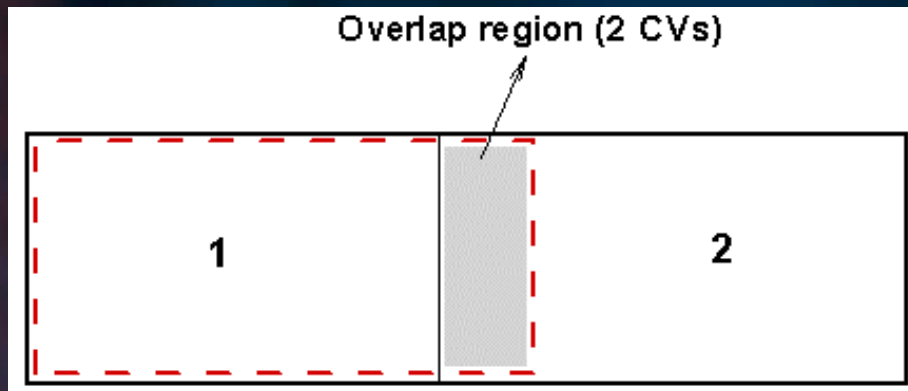
Multi-Block Finite Volume Scheme

- Domain Decomposition Technique



- Overlap between the blocks (sub-domains) for internal continuity.

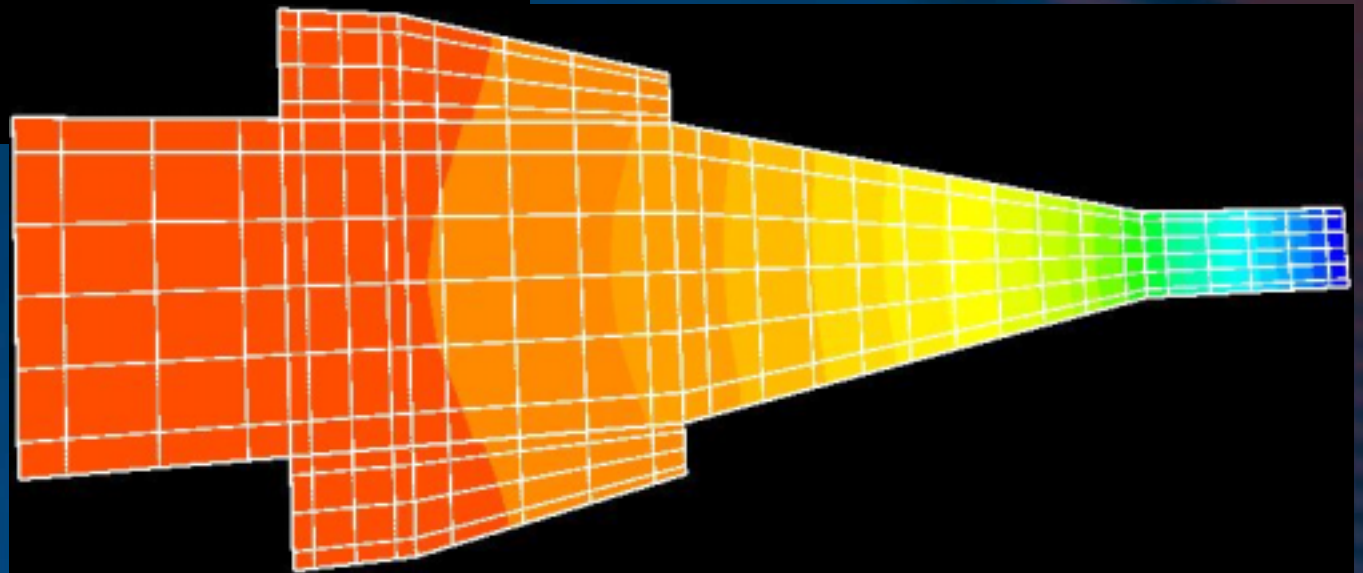
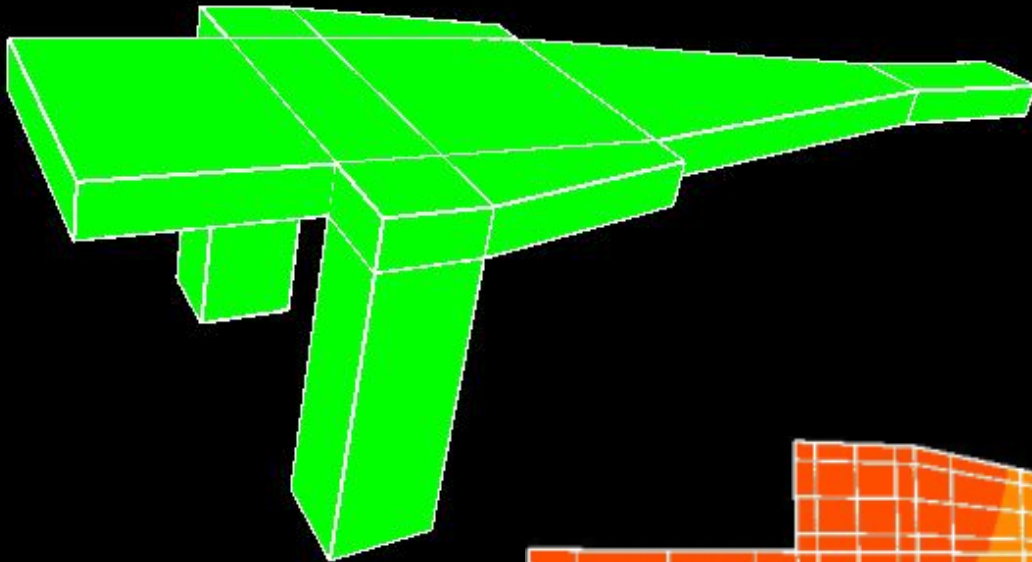
Multi-Block Finite Volume Scheme: Some Layouts



Multi-block Grid Generation

- **Independent grid system** in each block.
- Boundary-fitted coordinate (BFC) transformation to generate grids in each block.
- Structured, non-orthogonal grids provides high level of accuracy.
- Trans-Finite interpolation (TFI) for initial grids and then elliptic smoothener.
- Most appropriate for complex geometries
 - Can be split into geometrically simpler sub-domains.

Example : Multi-Block Mesh Generation



Multi-block Finite (Control) Volume Implementation

- Finite Volume scheme is most appropriate for fluid flow type problems.
 - Conservative formulation ensures accuracy.
 - Philosophy mimics actual physical phenomena.
- Coupled with multi-block strategy it can be used for complex geometries.
- Block calculations are independent – amenable to parallelization.
- Computationally more efficient for large problems as smaller matrices are solved for.
 - Performance of iterative solvers deteriorates with matrix size.

Generalized Conservative Formulation for Transport in Continua

- All relevant governing equations cast in a generic convection-diffusion form:

$$\frac{\partial \phi}{\partial t} + \nabla \cdot \vec{J} = S_{\phi}$$

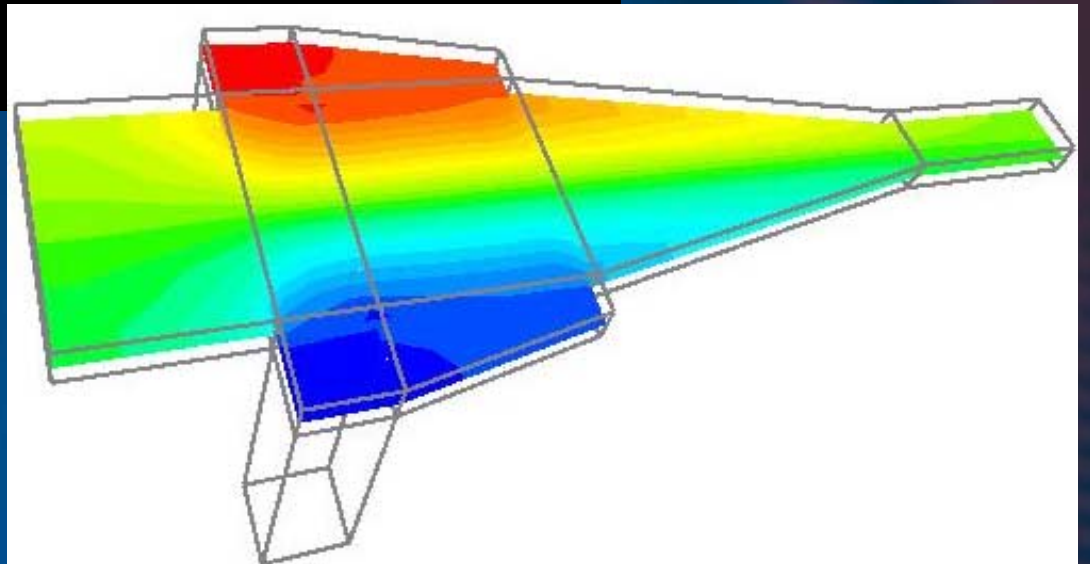
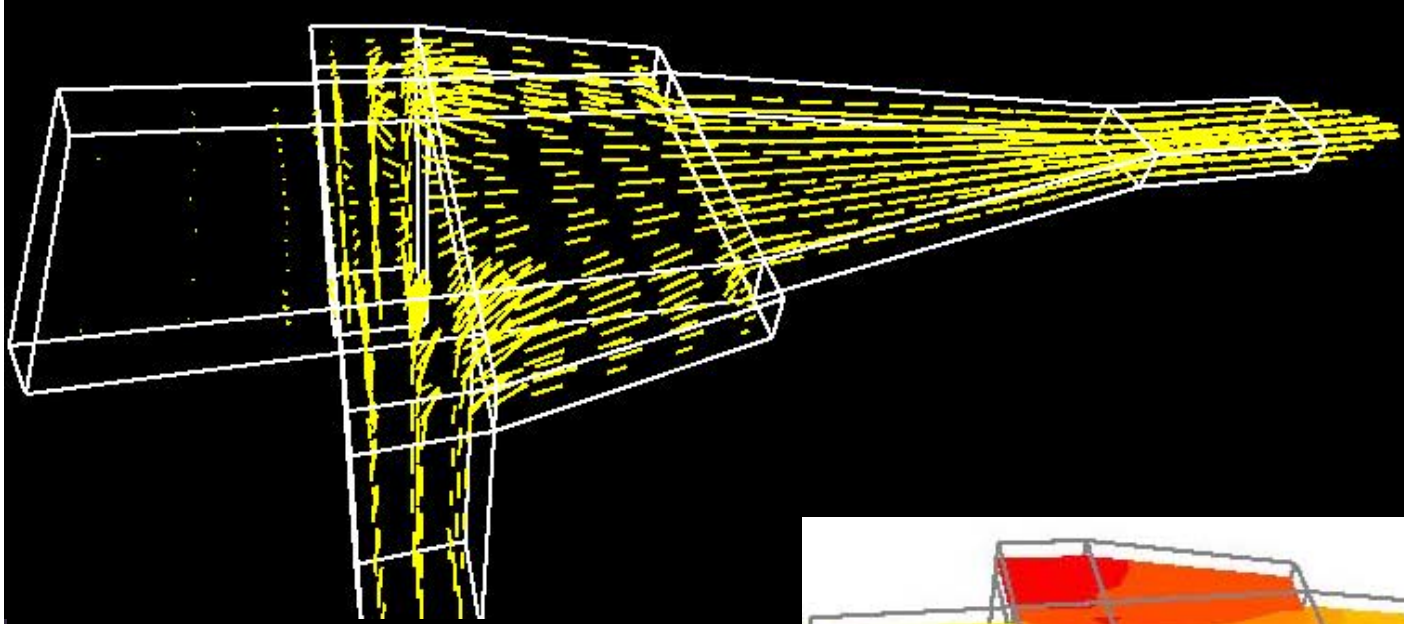
$$\vec{J} = \vec{U}\phi - \Gamma_{\phi}\nabla\phi + \vec{J}_{EK}$$

- \mathbf{J} is the total flux of dependent variable Φ .
- With appropriate choice of Φ and source S_{ϕ} , governing equation for all transport phenomena can be deduced.
 - Appropriate for physically complex problems.

Advantages of the Formulation

- Because of the generic nature it can account for the presence of multiple transport phenomena easily.
 - Conservation of solute mass, momentum, energy and current can be reduced to this form.
- Provides scalability and ease of algorithmic implementation.
 - Add/delete physical phenomena easily.

3D Mixer Problem



Transport Model for Analyte in Electrolyte Systems

- Central aspect of all **capillary electrophoresis** techniques and others like micro-array devices.
- Chemically active analytes undergo instantaneous association/dissociation reactions in the electrolyte system.
- Therefore, a coupled transport-stoichiometric modeling approach is needed.
- Further, this model should be for analytes of all types and valency in order to be practicable.

Generalized Association/Dissociation Model

- Strong analytes: undergo complete dissociation (e.g. HCl), fixed charge, easier to model.
- Weak analytes (general case):
 - Incomplete association/dissociation.
 - Can exist (co-exist) in both ionic and neutral states.
 - Ionic composition depends on local conditions like pH, etc.
- Analyte types:
 - Acid (anionic) : proton donors.
 - Base (cationic): proton acceptors.
 - Ampholytes: Can act as both acid and base depending on local pH, e.g. proteins.

Generalized Association/Dissociation Model

- Seek a stoichiometric model for **weak, multivalent** analyte of any type, which can be linked with transport model.
 - Valency of an analyte : max. number of dissociable protons.
- Any Analyte A with valency of n can exist in n+1 states, n ionic and 1 neutral (A_0, A_1, \dots, A_n).
- Corresponding reactions can be written compactly as



- And the dissociation constants ($j=n, n-1, \dots, 1$)

$$K_{n-j+1} = \frac{[A_{j-1}][H^+]}{[A_j]}$$

Generalized Association/Dissociation Model

- Treat the ensemble of all states (ionic and neutral) as one component variable in the formulation.
 - The reactions are instantaneous, infinitely faster than other transport processes.
- Total ensemble concentration of analyte $[A] = \sum [A_j]$
 - $[A_j]$ – concentration of ionic state with j protons.
- Using reaction kinetics models derive effective properties of the ensemble:
 - Effective charge $(z_{eff}) = F(z_i, K_i, [H^+])$
 - Effective mobility $(\Omega_{eff}) = F(\Omega_i, z_i, K_i, [H^+])$
 - Degree of dissociation of each state.

Coupling with Transport Equations.

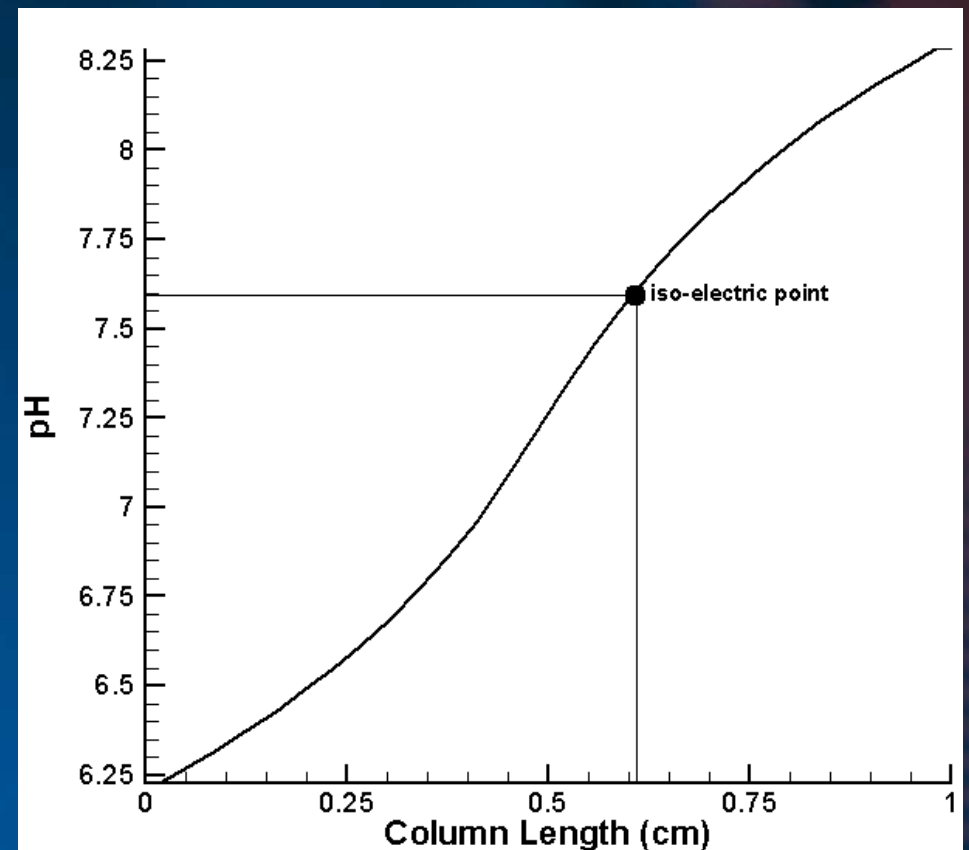
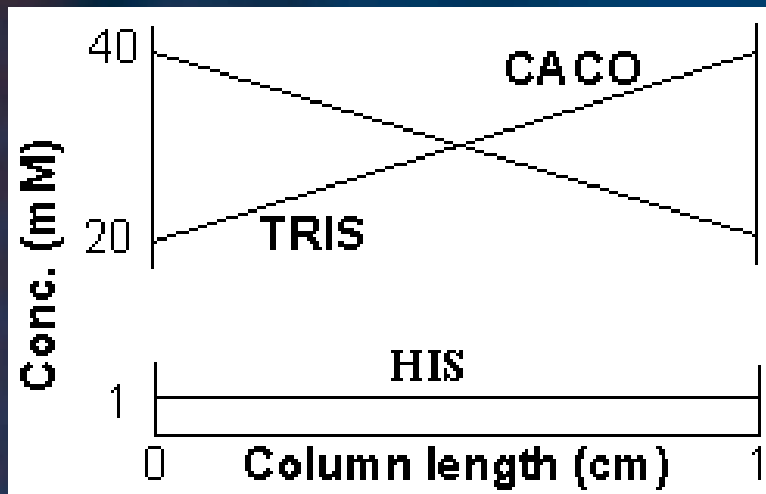
- The effective quantities calculated in the dissociation model can be used to calculate the total mass flux:

$$\vec{J} = \vec{U}[A] - D_A \nabla[A] - z_{eff} \Omega_{eff} [A] \nabla \Phi$$

- Other governing equations:
 - Current continuity for electric potential Φ .
 - Electroneutrality condition for pH.
- All governing transport equations are cast in the conservative convection-diffusion form.

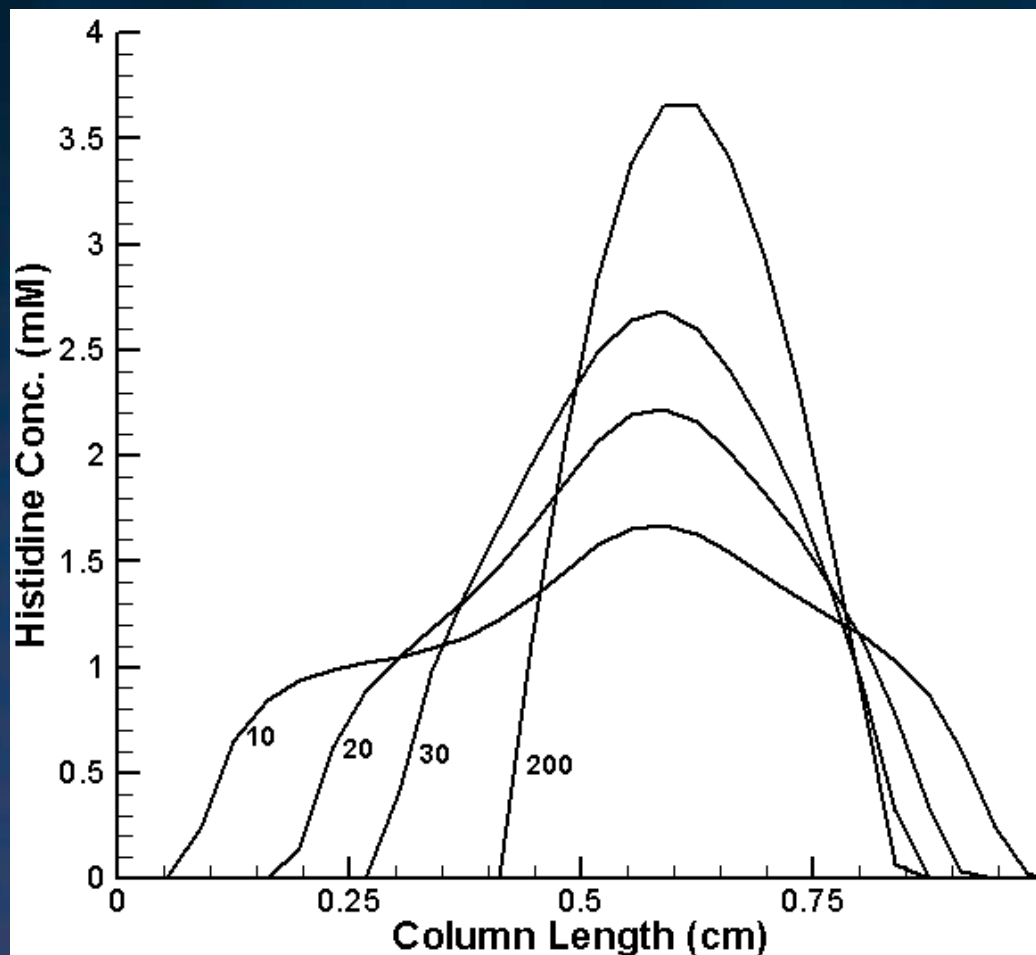
Capillary Iso-electric Focusing: No Bulk Flow

- Separation of ampholytes based on their isoelectric points.
- BGE : Cacodylic acid (CACO) and tris (hydroxylmethyl)-aminomethane (TRIS)
- Sample : Histidine



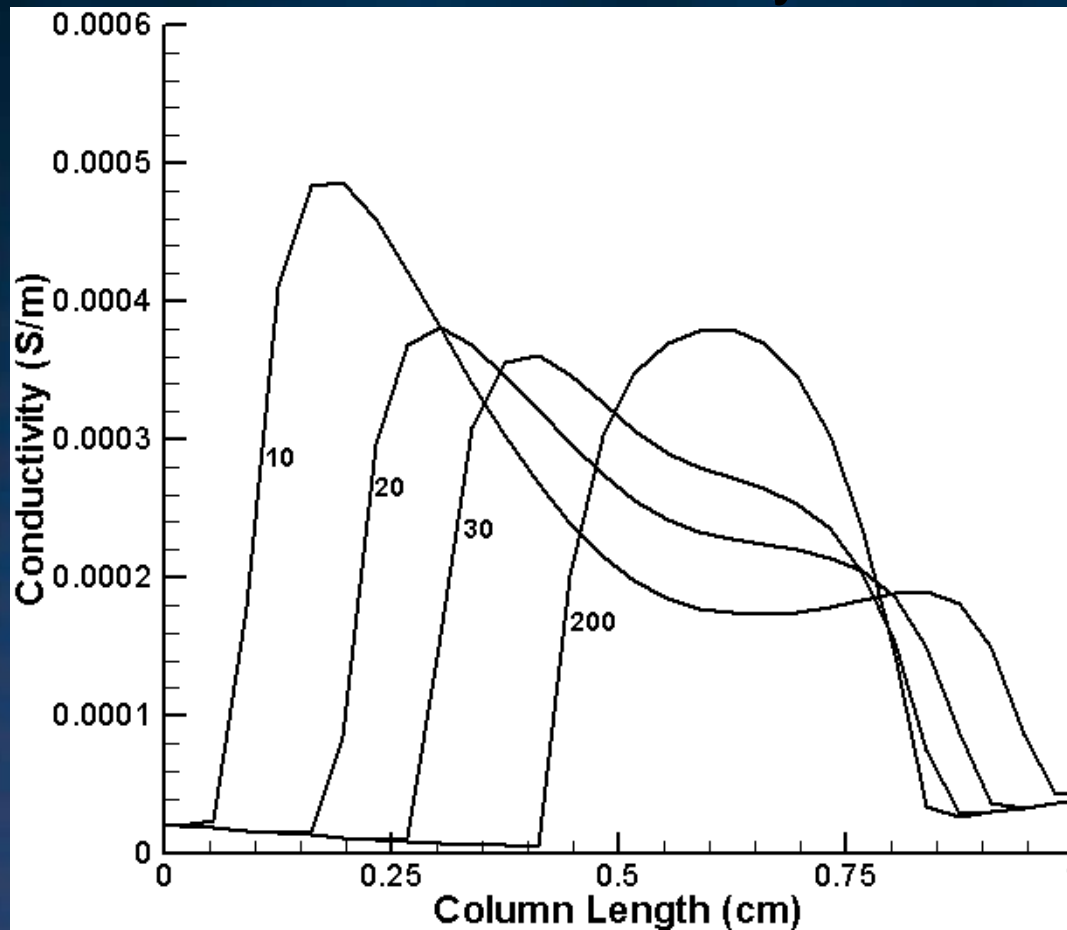
Capillary Iso-electric Focusing: No Bulk Flow

Transient Histidine Concentration profile ($I=0.2 \text{ A/m}^2$)



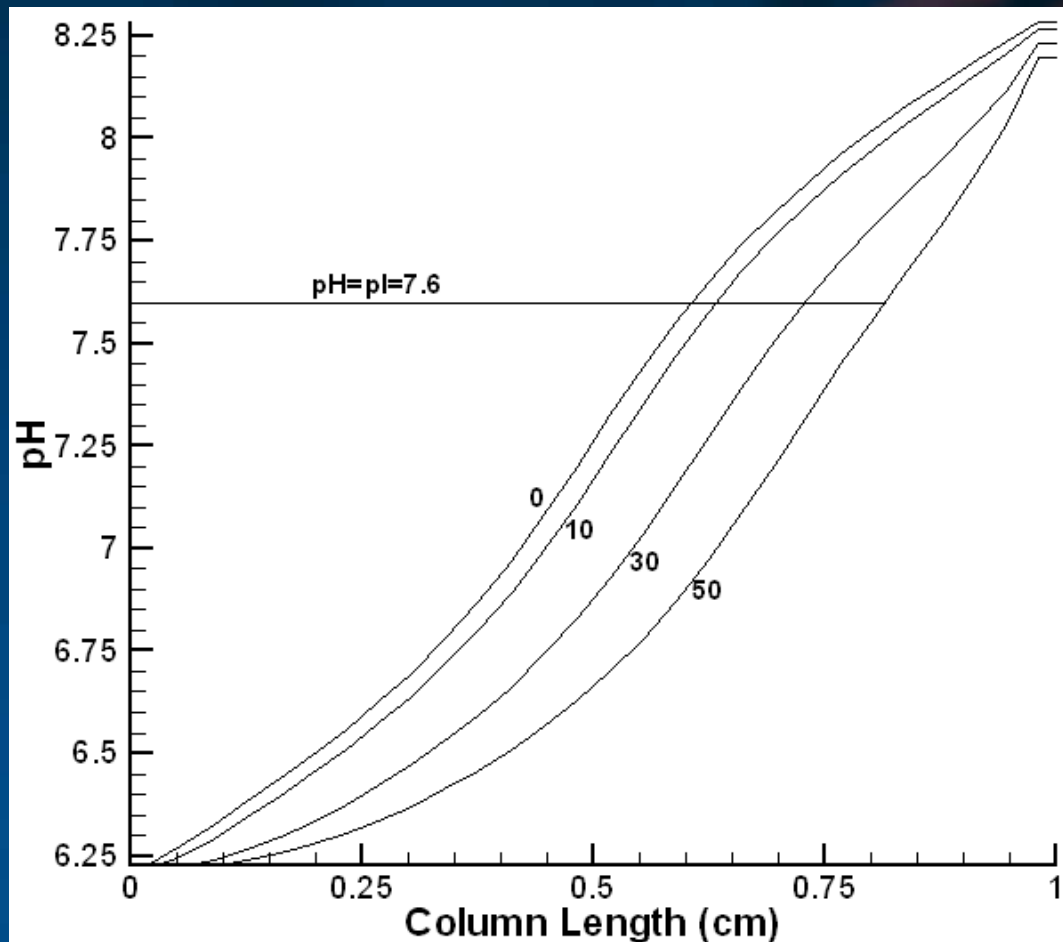
Capillary Iso-electric Focusing: No Bulk Flow

Transient Conductivity Profile



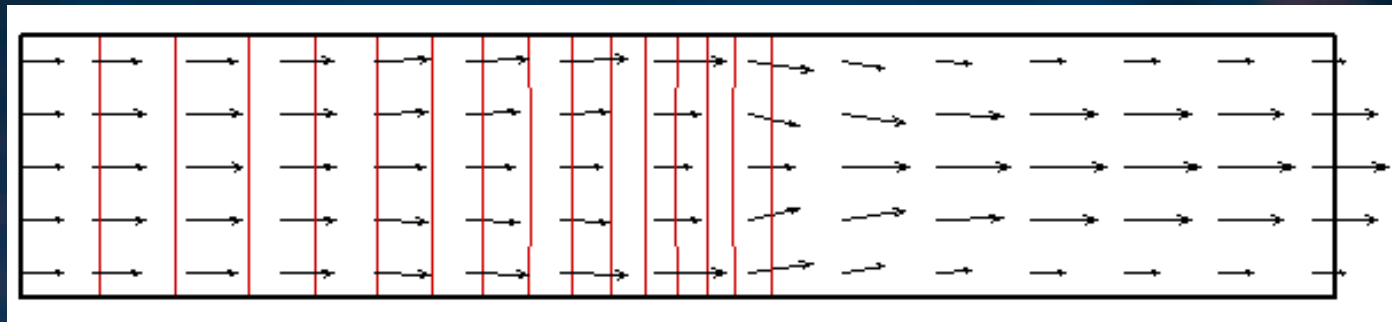
Capillary Iso-electric Focusing: With Bulk Flow

- Electroosmotic flow – zeta potential of -0.002 V.
- Transient pH profile.



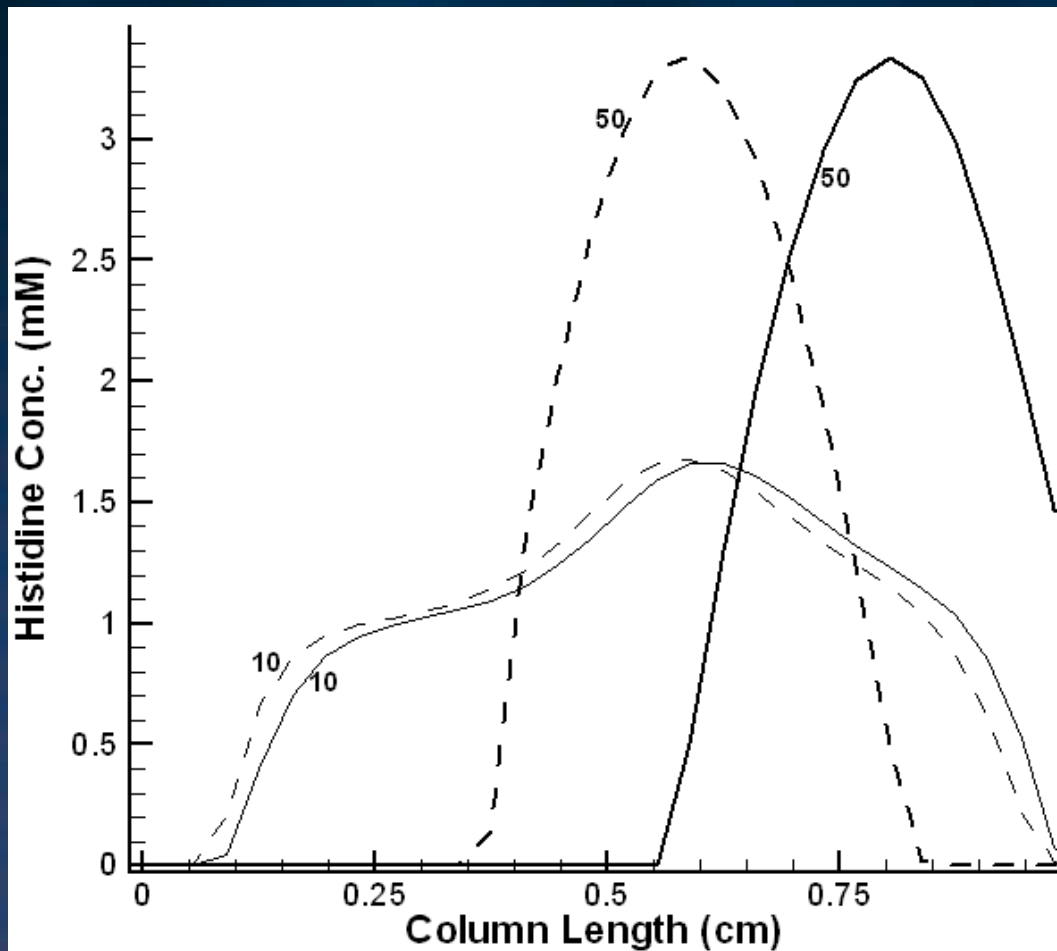
Capillary Iso-electric Focusing: With Bulk Flow

Non-uniform velocity field.



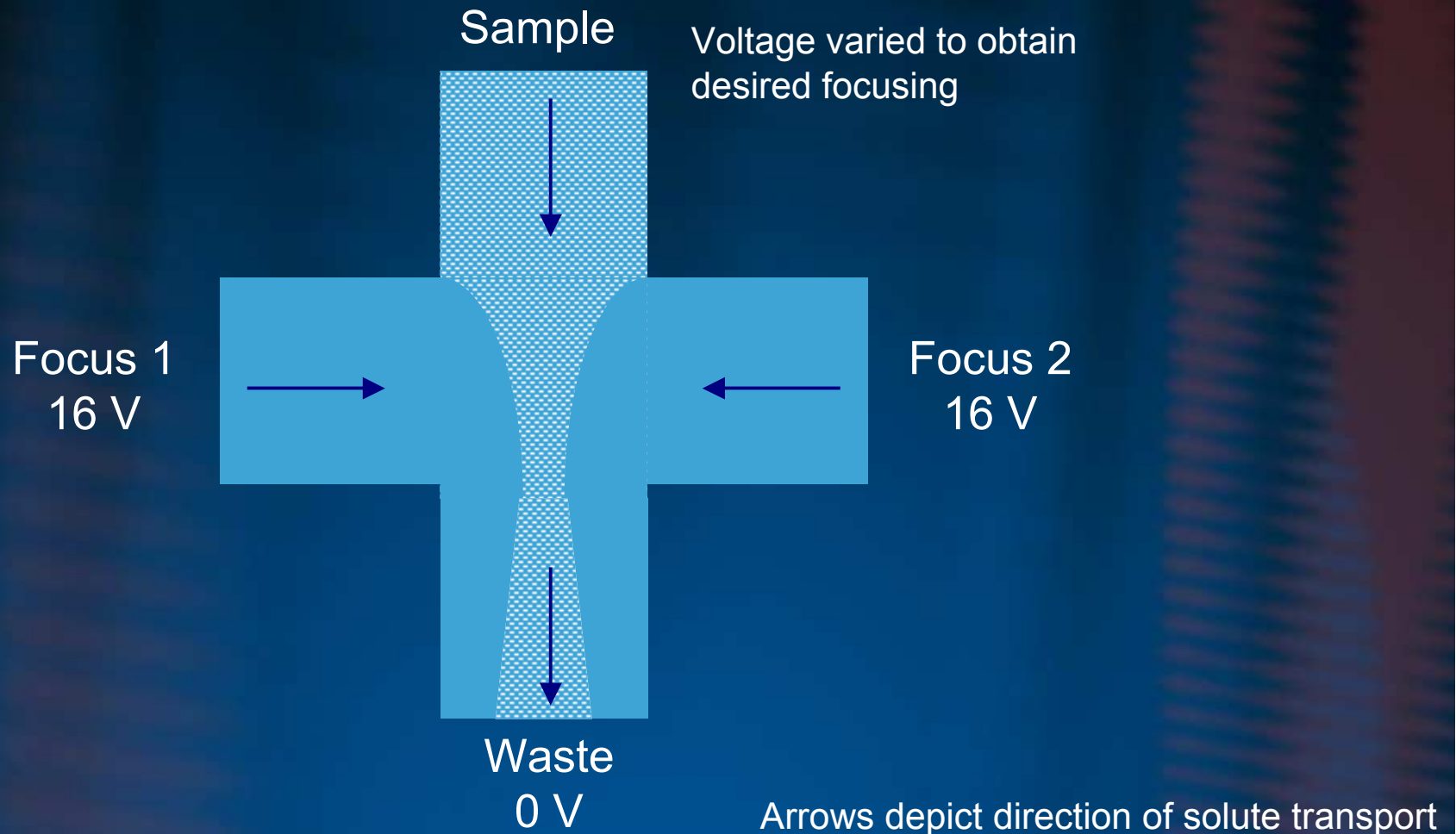
Capillary Iso-electric Focusing: With Bulk Flow

Transient Histidine concentration



IntelliSense

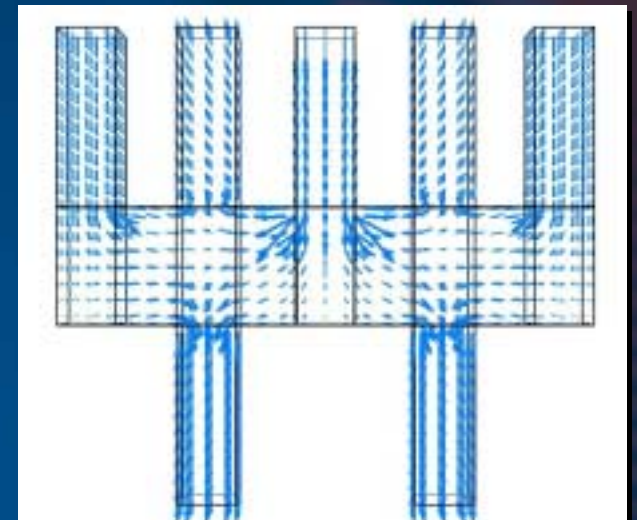
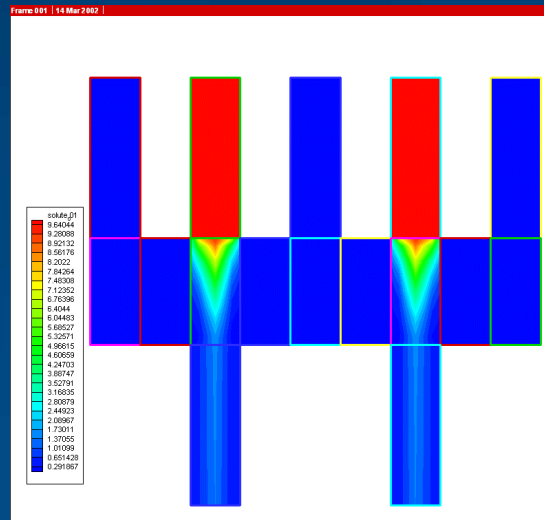
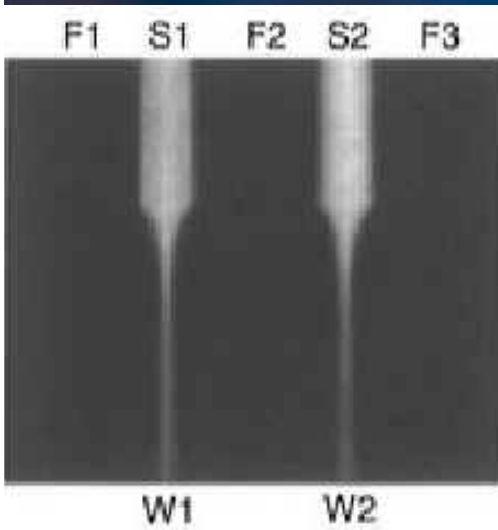
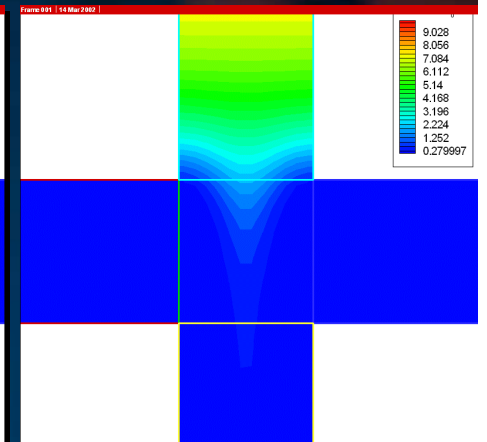
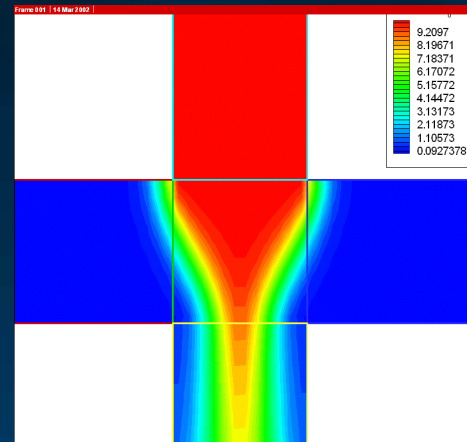
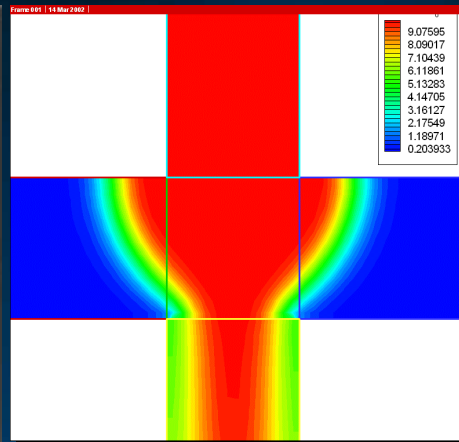
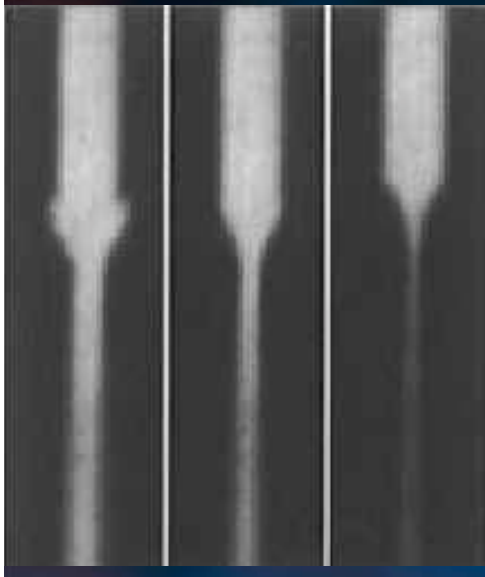
Electrokinetic Focusing Case Study



Electrokinetic Focusing Case Study

- Cross-channel configuration
 - Sample and waste channel lengths -100 μm
 - Focusing channel lengths - 60 μm
 - All channels are 18 μm in width and depth
- Buffer is a 10 mM Sodium Tetraborate solution
- Sample (cationic) is Rhodamine 6G (40 μM)
- Focusing reservoir is maintained at 16 V
- Waste reservoir is at ground
- Diffusivity is $3\text{e-}6 \text{ cm}^2/\text{s}$
- Electrophoretic mobility is $1.4\text{e-}4 \text{ cm}^2/(\text{V}\cdot\text{s})$
- Reference: Jacobson and Ramsey; Analytical Chemistry, Vol. 69, No. 16, August 15, 1997

Application: Electrokinetic Focusing



Conclusions

- **GENERALIZATION**: Valid for any analyte – multivalent, weak, and acid, base or ampholyte.
- Explicit coupling between transport phenomena and reaction kinetics.
- By virtue of ***generalized flux conservation*** formulation it can account for presence of multiple transport phenomena – bulk flow (pressure driven, EOM, etc.), electrophoretic effects, temperature effects, electric field calculations, etc.
- Generalized approach enables easy and efficient coupling with a variety of boundary conditions.
- Amenable to **parallelization**.