Multiphysics Simulation of Isoelectric Point Separation of Proteins Using Non-Gel Microfluidics System

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Mission

To nurture and harvest scientific creativity to produce life changing technologies
Discoveries

- Energy Storage through Electrochemistry
- Chemical/Biological Defense and Countermeasures
- Environmental Remediation
- Medical Technologies
Current Protein Diagnostic Techniques

Protein Analysis
- Enzyme-linked Immunosorbent Assays (ELISAs)
- 2D Gel Electrophoresis

Protein Detection
- Mass Spectrometer

Expensive
Immobile
Hard to Maintain
Slow
Remote Area Diagnostic

http://www.defenseindustrydaily.com

Yon M. Achieves. http://www.michaelyon-online.com

http://oregonstate.edu/dept/ncs

Lynntech
Song et al. from MIT’s Biological Engineering Laboratory designed PI based protein separation.

Lynntech’s Concept: Isoelectric Point based Protein Separation Chip

Objectives:
- High pH gradient at the exit of microfluidic channel.
- Multiple chip configuration that can achieve pH resolution of 0.1
Design of Experiments Procedure

Input parameter
Selection and range

Design of Experiments in JMP

Input design conditions of JMP in COMSOL and obtain model results

Evaluation criteria
• Maximum pH range coverage at the channel outlet.
  => \( E_1 = \text{pH}^A - \text{pH}^B \) = Maximum

• Most uniform pH distribution at the channel outlet
  => Uniform \( \frac{dpH}{dy} \)
  => \( E_2 = \text{Mean of } \frac{dpH}{dy} - \text{Std Dev of } \frac{dpH}{dy} \) = Maximum

Input evaluation criteria in JMP and analyze

Obtain optimized parameters

Check
**Design of Experiments**

**Plackett-Burman 12 Runs**

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<thead>
<tr>
<th>Number</th>
<th>Pattern</th>
<th>Top inlet pH</th>
<th>Top inlet ionic strength</th>
<th>Middle inlet pH</th>
<th>Middle inlet ionic strength</th>
<th>Bottom inlet pH</th>
<th>Bottom inlet ionic strength</th>
<th>L/over W ratio</th>
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<th>Flow rate</th>
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- This method is very economical and effective in understanding independent effect of each parameter.
COMSOL Model Set-up
Incompressible Navier-Stokes

\[
\rho \frac{\partial \mathbf{u}}{\partial t} - \nabla \cdot [\eta(\nabla \mathbf{u} + (\nabla \mathbf{u})^T)] + \rho (\mathbf{u} \cdot \nabla) \mathbf{u} + \nabla p = \mathbf{F}
\]

\[
\nabla \cdot \mathbf{u} = 0
\]

Inflow Velocity Pressure

Density=998 kg/m3 Dynamic Viscosity=1.002e-3 Pa-s

No Slip at the Wall

Subdomain Setting
Boundary Setting
COMSOL Model Set-up
Electrostatics

\[ \mathbf{D} = \varepsilon_0 (1 + \chi_e) \mathbf{E} = \varepsilon_0 \varepsilon_r \mathbf{E} \]

Diagram showing PDMS, Copper Electrode, Fluid Average Relative Permittivity, and Continuity.
COMSOL Model Set-up
Electrokinetics

\[
\frac{\partial c_i}{\partial t} + \nabla \cdot (- D_i \nabla c_i - z_i u_{mi} F c_i \nabla V + c_i u) = R_i
\]
COMSOL Results
pH Distribution at the Exit of the Channel
Statistical Optimization from COMSOL Results: Max pH

\[ f_1 = \Sigma_{(i=0,10)}(c_i \cdot p_i) \]

where \( f_1 \) = Maximum value of \( \Delta pH \),
\( c_i \) = constant, \( p_i \) = parameter
Statistical Optimization from COMSOL Results: Uniform pH

\[ f_2 = \sum_{i=0}^{10} (c_i \cdot p_i) \]

where \( f_2 \) = Maximum pH Uniformity, \( c_i \) = constant, \( p_i \) = parameter

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<tr>
<th>Term</th>
<th>Orthog Estimate</th>
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<td>Middle inlet pH</td>
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<td>L over W ratio</td>
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<td>Top inlet pH</td>
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<td>Bottom inlet pH</td>
<td>0.0130332</td>
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<td>L</td>
<td>0.0125747</td>
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<tr>
<td>Top inlet ionic strength</td>
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<td>Bottom inlet ionic strength</td>
<td>-0.0119458</td>
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<tr>
<td>Middle inlet ionic strength</td>
<td>0.0086563</td>
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COMSOL Results based on Statistical Analysis: No Potential Applied
COMSOL Results based on Statistical Analysis: Finite Potential Applied
Conclusions

Most dominant parameters controlling the process are identified.

An optimized design is proposed by numerical modeling.

pH gradient of range 1.5-13 with high uniformity is achieved.
Future Work

- Experimental Validation.
- Run DOE with more combination of few important parameters to fine tune the current design.
- Continue similar DOE for subsequent channels until a resolution of 0.1 is achieved.

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