Mathematical modeling for protein folding devices. Applications to high pressure processing and **microfluidic mixers**.

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Outlines

- Protein folding
  - Principle
  - Some interesting applications

- Microfluidic mixer optimization
  - Device description
  - Optimization Problem
  - Results

- Conclusions and perspectives
Part I: Protein folding
Definition

What are proteins? They are organic compounds (enzymes, DNA, ...) that catalyze chemical reactions (fermentation, vital support, ...).

For instance:

What is protein folding? It is a process that consists of a change in the protein structure from a folded state (can perform chemical reaction) to an unfolded state (inactive).

Representation:
Industrial applications

How protein folding process occurs? When energy is applied to protein provoking a perturbation of the protein conformational equilibrium. It can be performed, for instance, by using changes in temperature and/or pressure or changes in chemical potential (such as concentration changes).

What are the protein folding interests? The range of industrial applications is wide: DNA sequencing, drug molecules creation, food treatment, etc.
Interesting mathematical problems

Inside the consortium QUIMAPRES, we are interested in three main problematics:

- Design of microfluidic mixers: This part will be developed here.

- Modeling, simulation and optimization of High-Pressure/Temperature food treatment:


- Modeling and simulation of protein folding at chemical level: Work in progress (PhD).
Part II: Microfluidic mixer optimization
Device description

Principle: Microfluidic mixers are used to mix, as fast as possible, a protein solution with a solvent provoking a rapid change in chemical potential resulting in the unfold of certain proteins.

Example of microfluidic mixer: There exist a wide range of techniques to create microfluidic mixers.

For instance:

Considered mixer: Knight mixer
Knight mixer
Industrial problem

Objective: optimize the mixer to reduce the time needed to reach a certain protein concentration.

Previous work (collaborators: Stanford Microfluidics Lab.): A only shape optimization of the mixer have been done and validated by experiments: ‘Semi–deterministic and genetic algorithms for global optimization of microfluidic protein folding devices’, Intern. Journal of Num. Method in Engineering.

Current work: solve a more complex optimization problem considering more geometrical variables and the inlet velocities.
Shape parameterization

Center inlet

Side inlet

Axial symmetry

\( \Omega \)

Center inlet

Side inlet

Axial symmetry

\( \Omega \)

\( u_c \)

\( l_c \)

\( h_1 \)

\( l_1 \)

\( (c_{x1}, c_{y1}) \)

\( h_2 \)

\( l_2 \)

\( (c_{x2}, c_{y2}) \)

\( p_x \)

\( u_s \)

\( l_s \)

\( \theta \)

\( u_i \)

\( l_e \)
Mathematical modeling

Steady equations:

Navier–Stokes

+ Convective–Diffusion
Optimization problem

We are interested in minimizing:

\[ J(x_{\text{param}}) = \int_{c_{30}}^{x_{\text{param}}} \int_{c_{90}}^{x_{\text{param}}} \frac{dy}{u^{x_{\text{param}}}(y)} \cdot t, \]  

where \( c_{90} \), \( c_{30} \) and \( u^{x_{\text{param}}} \) are computed by solving numerically (considering a FEM) the following system:

\[
\begin{align*}
- \nabla \cdot (\eta(\nabla u + (\nabla u)^\top)) + \rho(u \cdot \nabla)u + \nabla p &= 0 \quad \text{in } \Omega, \\
\nabla \cdot u &= 0 \quad \text{in } \Omega, \\
\nabla \cdot (-D \nabla c + cu) &= 0 \quad \text{in } \Omega, \\
+ \text{boundary conditions.}
\end{align*}
\]

This optimization problem is solved by using the Global Optimization Platform software with a genetic algorithm as the core algorithm and where the initial population is generated using the secant method.
Some results

![Graph showing concentration over time and x-coordinate.]

- Initial time
- Mixing time

**Conclusions and perspectives**
Conclusions and perspectives
Conclusions and perspectives

- Importance of the protein folding process in *industrial applications*.
- For each application, our modeling/simulation are validated by posteriori prototyping.
- The new parameterization allows to improve existing microfluidic mixers.

**Perspectives:** Direct modeling of the folding process, creations of new patents...
Conclusions and perspectives

Global Optimization Platform

http://www.mat.ucm.es/momat/software.htm
Conclusions and perspectives

!!! Thank You !!!