

CHEM420 Selected Topics in Analytical Chemistry

Analytical Applications of Microfluidics

Lecture 4: Mixing part 1

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Lecture 3 Summary

- ▶ **Poiseuille Flow** - pressure driven, steady state flow
 - ▶ valid for $Re \rightarrow 0$
 - ▶ **pressure boundary condition** imposes Δp across channel inlet and outlet
 - ▶ **non-slip boundary condition** means $\mathbf{v} = 0$ at all points on channel boundary
 - ▶ velocity varies across channel section! Distribution in residence times
- ▶ **Hagen-Poiseuille Law** is Ohm's law for fluidics

$$\Delta p = R_{hyd} Q$$

- ▶ **hydraulic resistance** related to channel cross section and length
- ▶ **hydraulic compliance** related to volume change of channel, tube, or bubble
- ▶ consider response time τ of system for given measurement technique

Motivation: Real Devices

We have spent a lot of time studying the properties of **fluid flow**:

- ▶ Navier-Stokes and Continuity equations are **governing equations for fluid mechanics**
- ▶ Reynolds number Re captures the **flow regime** based on fluid and channel properties
- ▶ In microfluidics, Re is low and flow is **laminar** i.e. orderly and without turbulence
- ▶ We can analyze device layouts using the **Hagen-Poiseuille Law**

But we're chemists! We also want to study **mass transport** i.e. how molecules or particles move through microfluidics

Diffusion: Fick's First Law

Let $c(\mathbf{r}, t)$ be a scalar field describing the concentration of a solute at position \mathbf{r} and time t . (We'll write c for short.)

For *low concentration solutions* in a *homogeneous and isotropic medium*, we can describe diffusion flux with **Fick's First Law**:

$$\mathbf{J} = -D\nabla c \quad \text{Fick's First Law}$$

where

- ▶ \mathbf{J} is *flux* of solute (units $\text{mol m}^{-2} \text{s}^{-1}$)
- ▶ D is diffusion coefficient (units $\text{m}^2 \text{s}^{-1}$)
- ▶ ∇c is concentration gradient (units $\text{mol m}^{-3} \text{m}^{-1}$)

Fick's First Law says that there is a net flux (i.e transport due to diffusion) wherever there is a concentration gradient.

Diffusion: Fick's Second Law

Fick's First Law just describes flux \mathbf{J} (amount of mass flowing through unit area per unit time.) We want how c itself changes with time. For that, we need **Fick's Second Law**:

$$\frac{\partial c}{\partial t} = D \nabla^2 c \quad \text{Fick's Second Law}$$

where

► $\nabla^2 = \nabla \cdot \nabla$ is Laplace operator

This says that concentration increases or decreases fastest in locations where concentration gradient is steepest.

Note the difference: First Law describes how *flux* changes, Second Law describes how *concentration* changes.

Diffusion: Fick's Second Law

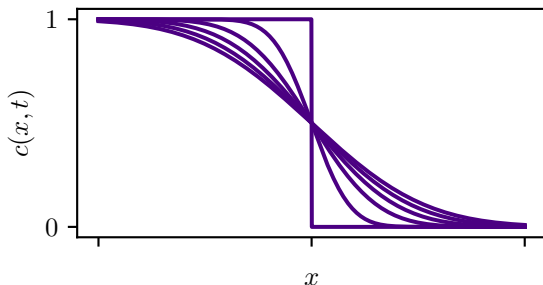


Figure: 1-D diffusion

Can define characteristic length and time for diffusion:

- ▶ diffusion length $L = \sqrt{DT}$ over characteristic time T
- ▶ diffusion time $T = \frac{L^2}{D}$

Diffusion Coefficients

Particle	Typical Size	Diffusion Coefficient (m s^{-2})
<i>solute ion</i>	0.1 nm	2×10^{-9}
<i>small protein</i>	5 nm	4×10^{-11}
<i>virus</i>	100 nm	2×10^{-12}
<i>bacterium</i>	1 μm	2×10^{-13}
<i>human cell</i>	10 μm	2×10^{-14}

Advection

Transport of solutes by fluid flow is called **advection**. Mathematically, we write the change in concentration due to advection as

$$\frac{\partial c}{\partial t} = -\mathbf{v} \cdot \nabla c \quad \text{Advection equation}$$

Intuition: Advection “stretches” concentration distributions

Example

Advection of a pulse of dye in Poiseuille flow.

The Advection-Diffusion Equation

$$\frac{\partial c}{\partial t} = D \nabla^2 c - \mathbf{v} \cdot \nabla c \quad \text{Advection-Diffusion Equation}$$

Governing equation for mass transport in fluid flow. Note that adding source term R turns this into Advection-Diffusion-Reaction Equation.

Key point: Two contributions to mass transport in microfluidics:

1. *Diffusion* - mass transport due to *concentration gradients* (technically chemical potential gradients)
2. *Advection* - mass transport due to *underlying solvent motion*

(Chickens on a bus analogy.)

Non-dimensionalizing the Advection-Diffusion Equation

Recall: When we non-dimensionalized the Navier-Stokes equation, the Reynolds number popped out! What happens when do that for Advection-Diffusion Equation?

$$\frac{\partial c}{\partial t} = D \nabla^2 c - \mathbf{v} \cdot \nabla c \quad \text{Advection-Diffusion Equation}$$

Example

Non-dimensionalize the terms in the A.D.E. using the following scales:

$$c = C_0 \tilde{c} \quad t = \frac{L_0^2}{D} \tilde{t} \quad \mathbf{v} = V_0 \tilde{\mathbf{v}}$$

$$\frac{\partial}{\partial t} = \frac{D}{L_0^2} \frac{\partial}{\partial \tilde{t}} \quad \nabla = \frac{1}{L_0} \tilde{\nabla} \quad \nabla^2 = \frac{1}{L_0^2} \tilde{\nabla}^2$$

Peclet Number

$$\frac{\partial \tilde{c}}{\partial \tilde{t}} = D \tilde{\nabla}^2 \tilde{c} - \text{Pe} \tilde{\mathbf{v}} \cdot \tilde{\nabla} \tilde{c}$$

$$\text{Pe} = \frac{V_0 w}{D} \quad \text{Peclet Number}$$

Dimensionless quantity which describes ratio of advective to diffusive transport. Typically the channel width w (or hydraulic diameter D_h) is taken as the critical length.

Two regimes...

1. $\text{Pe} < 1$ - **diffusion dominates** over advection
2. $\text{Pe} > 1$ - **advection dominates** over diffusion

Example

Compute the Peclet number for ferrocyanide in 0.1 M KCl ($D = 0.7 \times 10^{-9} \text{ m}^2/\text{s}$) in a microfluidic with average velocity $V_0 = 0.1 \text{ mm/s}$ and width $w = 500 \text{ }\mu\text{m}$. What transport mechanism dominates?

Answers: $\text{Pe} = 71$. Advection dominates.

A very simple “mixer”: the T-mixer

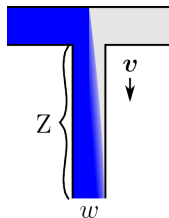


Figure: The T-mixer. A stream of solute (blue) with diffusion coefficient D meets pure solvent (grey) and the two streams co-flow to the outlet with average velocity V_0

Time required to diffuse across width: $T \approx w^2/D$

Distance travelled down channel in that time: $Z = V_0 T = V_0 w^2/D$

Define **Peclet number** Pe as the number of channel widths required for complete mixing $Pe = \frac{Z}{w} = \frac{V_0 w}{D}$

Allows precise control of fluid transport and study of transport properties

Back to a previous example...

Let's return to the previous example with a new question.

Example

The Peclet number for ferrocyanide in 0.1 M KCl ($D = 0.7 \times 10^{-9} \text{ m}^2/\text{s}$) in a microfluidic with average velocity $V_0 = 0.1 \text{ mm/s}$ and width $w = 500 \text{ }\mu\text{m}$ is $\text{Pe} = 71$. What channel length is required for complete mixing?

Answer: 36.5 mm

Application: T-mixers in analytical chemistry

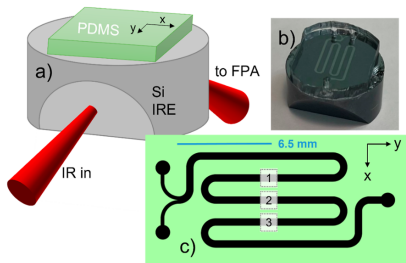


Figure: T-mixer integrated with FTIR internal reflection element. Device dimensions are $w = 500 \mu\text{m}$, $h = 38 \mu\text{m}$, $L \approx 60 \text{ mm}$. Device constructed out of PDMS and silicon in SyLMAND. FTIR FPA images collected at positions 1, 2, 3

Flaman *et al.* Analytical Chemistry 2023

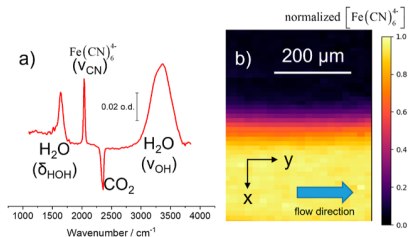


Figure: a) Example spectrum of ferrocyanide in water with band assignment. b) FPA image of ferrocyanide diffusion into water at position 2.

Application: Comparison of experiment to theory

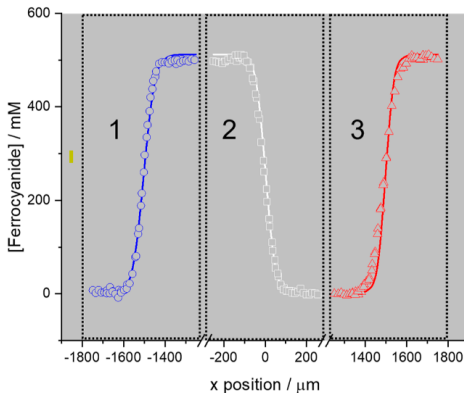


Figure: Comparison of experimentally obtained image (circles) extracted from FPA image and numerical solution of ADE (solid line) with COMSOL.

Proof of principle of quantitative measurement of diffusion profiles with coupled analytical and microfluidic methods.

Application: Separation based on Peclet number

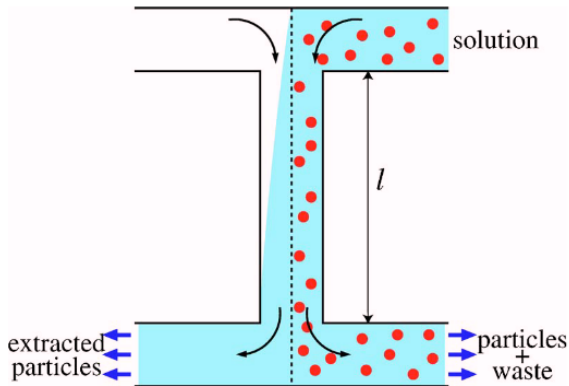


Figure: Separation on the basis of differing D . A solution charged with two solutes, with D_1 and D_2 , meets a stream of neat solvent. If $D_1 > D_2$, it will diffuse faster into the neat solvent and can be extracted. Adapted from Quake & Squires.

How an H-filter works

Note: H-filters have $w \gg h$ so that velocity profile is essentially flat across width. (Recall Poiseuille flow results from Lecture 3).

Two critical times in H-filter: diffusion time τ_{diff} and advection time τ_{adv} :

$$\tau_{diff} = \frac{(w/2)^2}{D} = \frac{w^2}{4D} \quad \tau_{adv} = V_0 L$$

Solutes with $\tau_{adv} \ll \tau_{diff}$ will not have enough time to diffuse and will flow to waste. But, if $\tau_{adv} \approx \tau_{diff}$ then diffusion occurs and solute fills the extracted stream.

Example

What is the critical value of diffusion coefficient, D^* , where complete mixing happens? What implication does this have for an H-filter?

Answer: $D^* = V_0 w^2 / 4L$

Using Pe to design an H-filter

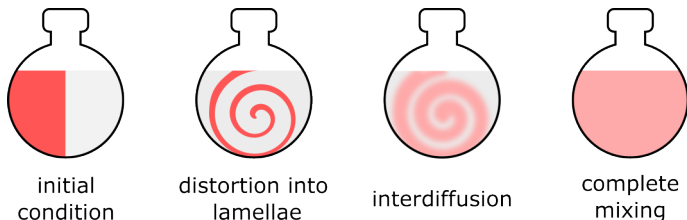
As shown in a previous example, Pe can be interpreted as the number of channel widths required for complete mixing. Because a solute only needs to traverse half the channel width, can write an effective Peclet number

$$Pe_H = \frac{V_0 w / 2}{D} = \frac{V_0 w}{2D}$$

But wait... none of this looks like mixing as we're used to it!

What if we want to mix faster than diffusion alone?

A cartoon version of mixing



Macroscopic mixing occurs by a mix of *advection* and *diffusion*. The two fluids are deformed by an external force (e.g. stir bar) into layers (lamellae). Fluids (or solutes) in the lamellae interdiffuse, decreasing local concentration gradients. At long time, diffusion homogenizes the concentrations.

Key point: Diffusion is a slow process; decreasing diffusing length and surface contact area by “laminating” fluids together significantly speeds up mixing!

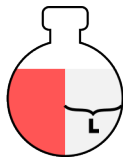
Equivalent ways to improve mixing

Option 1: Total Flux Integrating flux over all interfacial area A over which diffusion occurs, can find total flux J_{total} :

$$J_{total} = D \cdot A \cdot \nabla c$$

D is constant (mostly). Maximize interfacial area A or concentration gradient ∇c to maximize mixing.

Option 2: Decrease Diffusion Length Diffusion length $L \propto t^{1/2}$ - diffusing occurs much faster over short length scales! So decrease distance over which diffusion is needed.



long diffusion length
low interfacial area A
slow mixing



short diffusion length
high interfacial area A
rapid mixing

Interdigital mixers

Concept: mix two fluids A and B by laminating many different thin streams together. Increase A , decrease L .

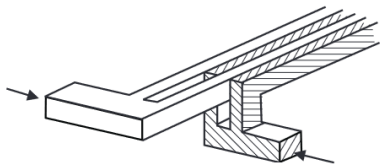


Figure: Interdigital mixing concept. Note 3D geometry is highly challenging to fabricate with conventional microfab methods; often off-chip fluid manifolds are required. Nguyen & Wu, J. Micromech. Microeng. 2005

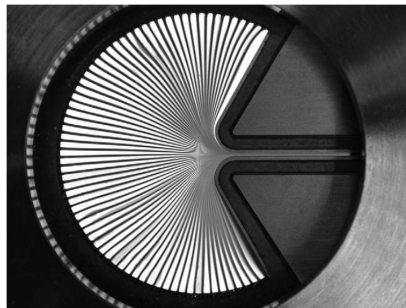


Figure: 138 channel interdigital mixer. 4 ms mixing time achieved with 4 μm lamellae widths. Stainless steel, 3.5 bar operating pressure. Hell yeah! Löb et al. Chem. Eng. Tech. 2004

Mixing at low Re

Concept: for $Re = 1$ to 100 the staggered herringbone mixer (SHM) allows mixing length to scale with $\ln(Pe)$, not Pe as in T-mixer!

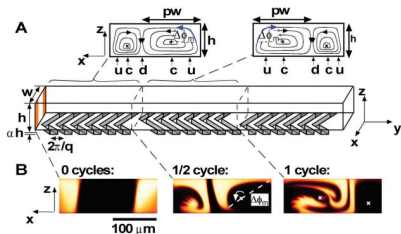


Figure: (A) SHM layout showing counter-rotating flow vortices induced by directional change in resistance along herringbone peaks. (B) Confocal optical microscopy of dye. Stroock *et al.*, Science 2002

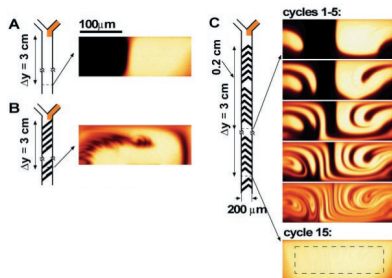


Figure: Effect of multiple SHM cycles on dye solution.