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November 1, 2013

Inverse Problems in the Biosciences: Introduction, Mathematical Issues, Solution Approximation and Analysis.

The goal of an interdisciplinary mathematician, inspired by NSF-DMS Mathematical Biology, is to make contributions to both an outside discipline as well as Mathematics.

In this talk will provide an

(I) **Introduction to Inverse Problems**.

(II) **Identification of Ion Channel Distributions in Olfactory Cilia**.

(III) **Inverse Problems in HIFU/MRI** – Beginnings.

(IV) **Attachment/Detachment in Biofilms in Urban Pipes** – Beginnings.

Biomedical Engineering Survey (BME 7001), 648 Baldwin Hall, 11 AM, Nov. 7, 2013.

Inverse Problems – Introduction (Groetsch, Viewig (1993)):

An inverse problem is a problem which is posed in a way that is inverted from that in which most direct problems are posed.

Example Inverse Problem: Find rate r in population, $P = P(t)$ in millions, growth model;

$$\frac{dP}{dt} = rP \quad \text{with initial condition } P(0) = 5 \text{ and } \textbf{Extra} \text{ condition } P(1) = 10.$$

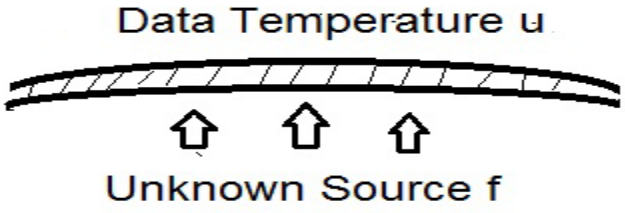
Simple since solution is known,

$$P(t) = P_0 \exp(rt)$$

Initial condition gives $P_0 = 5$ so

$$10 = 5 \exp(r \cdot 1) \quad => \quad r = \ln(2)$$

Partial Differential Equation Example Inverse Problem:



Model by 1-D Heat Conduction I/BVP:

$$\frac{\partial u}{\partial t} = \frac{\partial^2 u}{\partial x^2} + f \qquad \text{BC } u(0,t) = u(\pi,t) = 0 \qquad \text{IC } u(x,0) = 0.$$

Task: Given data on u, determine an approximation for the source function f.

Naive Approach: Create approximations of $\partial u/\partial t$ and $\partial^2 u/\partial x^2$ from least squares fit to u.

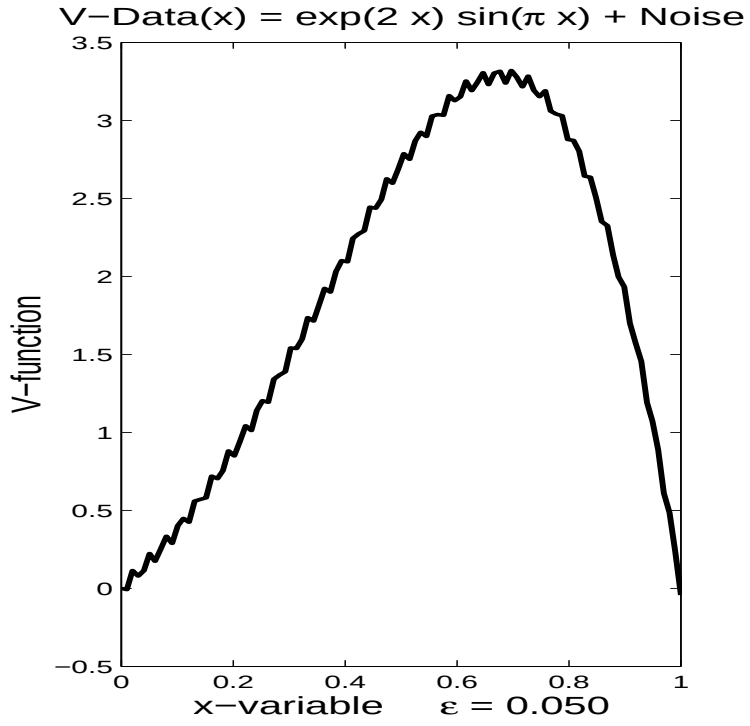
Data and Derivatives: Suppose

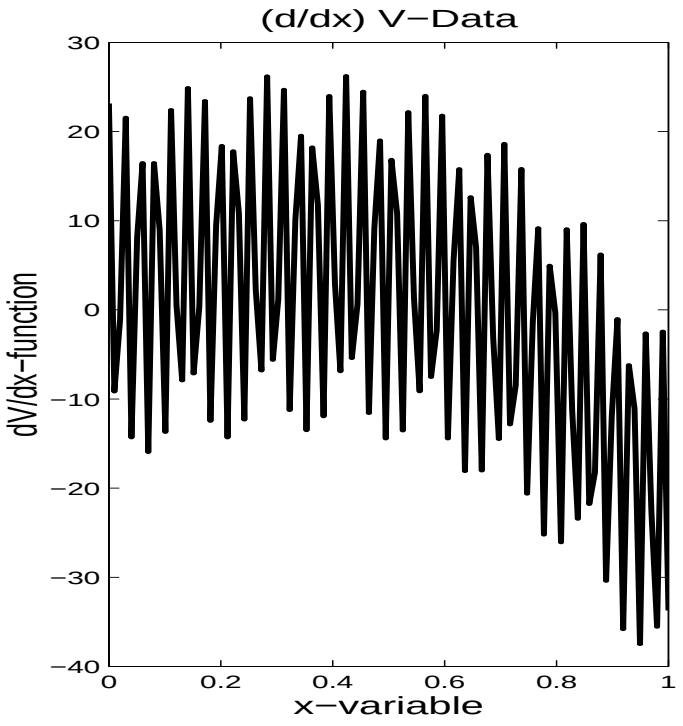
$$V_{Data}(x) = V(x) + \epsilon \sin(x/\epsilon^2) \quad \text{and thus} \quad V'_{Data}(x) = V'(x) + (1/\epsilon) \cos(x/\epsilon^2)$$

where $V(x)$ is a smooth function and the sine term represents noise and data errors. Note

$$\max_{s\in\mathbf{R}} |V_{Data}(s) - V(s)| \leq \epsilon \qquad \max_{s\in\mathbf{R}} |V'_{Data}(s) - V'(s)| = O(1/\epsilon).$$

Conclusion: Avoid the direct approximation of derivatives from function data.





Another Challenge - Ill-Posedness: Solution f does not depend continuously on data for u.

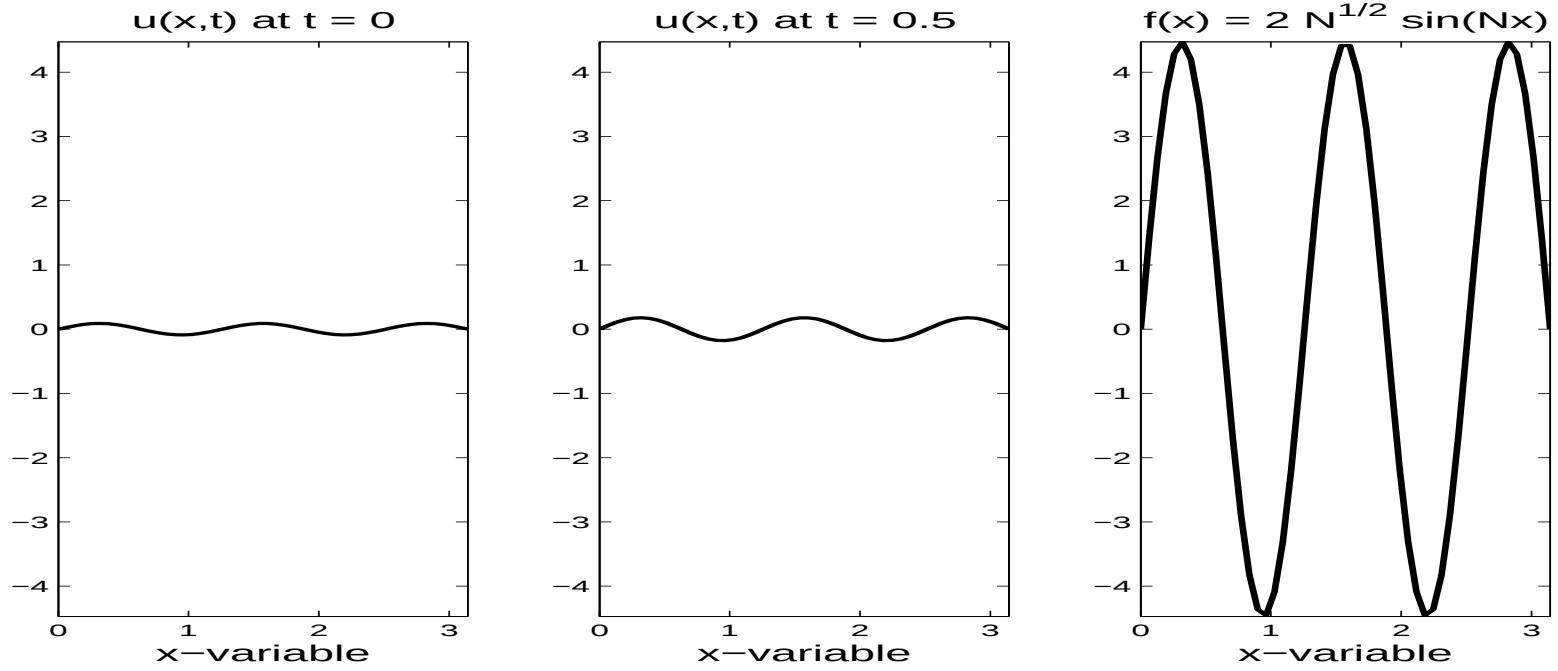
$$\frac{\partial u}{\partial t} = \frac{\partial^2 u}{\partial x^2} + f \qquad \text{BC } u(0,t) = u(\pi,t) = 0 \qquad \text{IC } u(x,0) = 0.$$

Example: Suppose N is a large positive integer.

Function $u(x,t) = N^{-3/2}(2 - e^{-N^2 t}) \sin(Nx)$ satisfies PDE with $f(x,t) = 2\sqrt{N} \sin(Nx)$.

(So $u(0,t) = u(\pi,t) = 0$ and $u(x,0) = O(N^{-3/2})$ small.)

Then $u \to 0$ does not imply $f \to 0$ as $N \to \infty$.



Back to the 1-D Heat Conduction I/BVP:

$$\frac{\partial u}{\partial t} = \frac{\partial^2 u}{\partial x^2} + f \qquad \textbf{BC } u(0,t) = u(\pi,t) = 0 \qquad \textbf{IC } u(x,0) = 0.$$

Assuming (Fourier Series)

$$f(x,t) = \sum_{n=1}^{\infty} f_n(t)\sin(nx) \qquad \text{with} \qquad f_n(t) = \frac{2}{\pi}\int_0^{\pi} f(y,t)\sin(ny)\, dy$$

then (Separation of Variables)

$$u(x,t) = \sum_{n=1}^{\infty} c_n(t)\sin(nx) \qquad \text{with} \qquad c_n(t) = \int_0^{t} e^{-n^2(t-s)} f_n(s)\, ds.$$

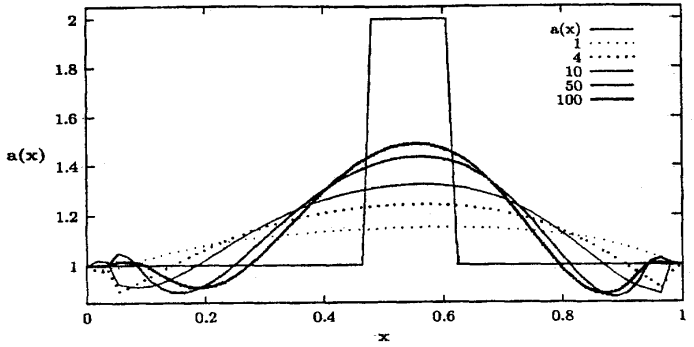
Integral Equation Representation: (Avoids derivative troubles).

$$u(x,t) = \int_0^t \int_0^{\pi} k(x,y,t-s) f(y,s)\, dyds \quad \text{with} \quad k(x,y,\tau) = \frac{2}{\pi}\sum_{n=1}^{\infty} e^{-n^2\tau}\sin(nx)\sin(ny)$$

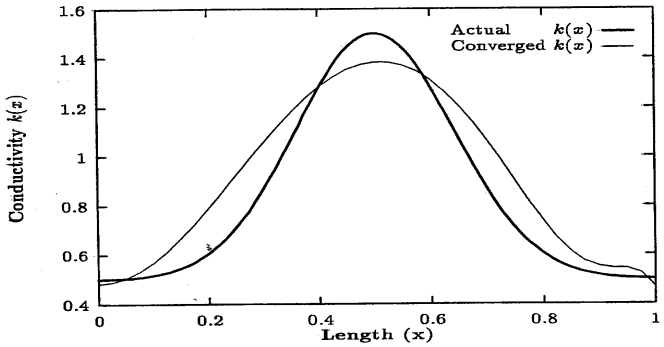
Approximation of f by finite difference or element leads (Again, given data on u) to an ill-conditioned system of equations $A\vec{F} = \vec{U}$. (**Tikhonov Regularization** can help with this.

Inverse Problem Results from the Literature:

Absorption $a(x)$ in [TKC]



Conductivity $k(x)$ in Tadi



Tadi, Klibanov, and Cai (2002): Unknowns $u = u(x,t)$ and $a = a(x)$.

$u_t - u_{xx} + au = 0$ BC $u(0,t) = 0.1$ and $u_x(1,t) = f(t)$ IC $u(x,0) = 0.1$

"Extra BCs:" $u_x(0,t) = y_1(t)$ $u(1,t) = y_2(t)$

Tadi (1997): Unknowns $T = T(x,t)$ and $k = k(x)$.

$T_t = (kT_x)_x$ BC $T(0,t) = 0.1$ and $kT_x(1,t) = f(t)$ IC $T(x,0) = 0.1$

"Extra" BC: $T(1,t) = y(t)$

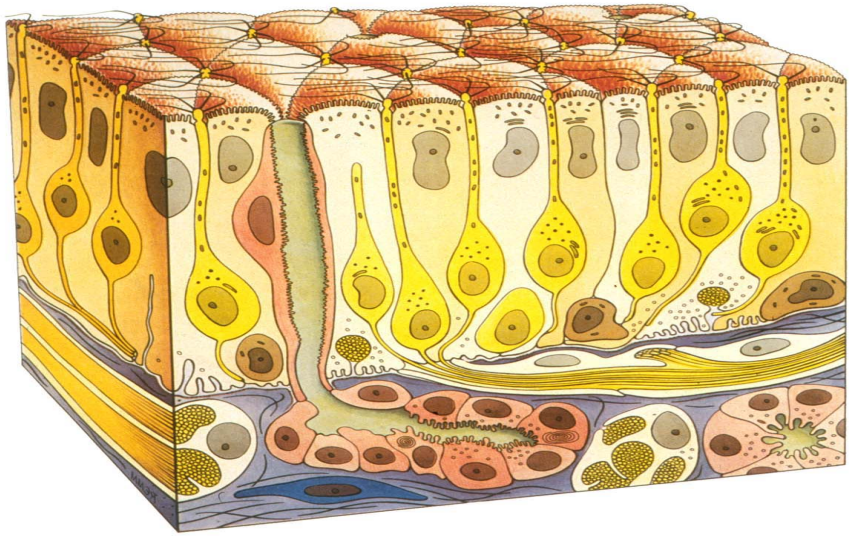
Inverse Problems in Olfaction Experimentation

Identification of ion channel distributions in frog olfactory cilia

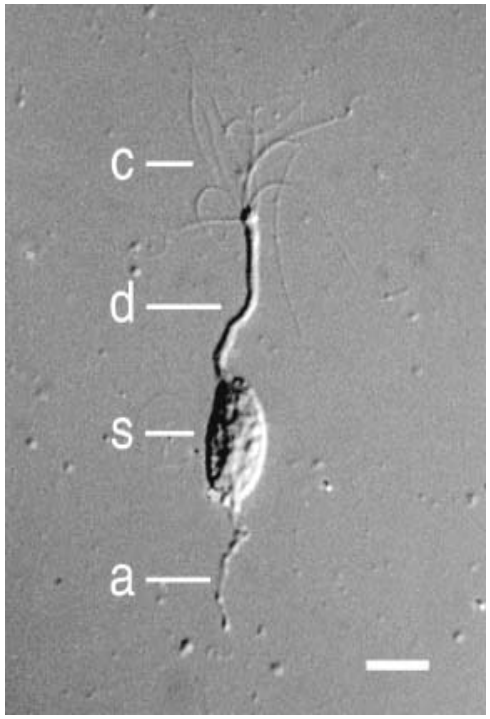
With S.J. Kleene (College of Medicine)

Cilia are long thin processes that extend from the olfactory receptor neurons. The first step in the transduction of an odor into an electrical signal occurs in the membranes of the cilia and is controlled primarily by ion channels. In this study, Mathematical models and simple approximation methods are derived to obtain estimates of the spatial distributions of the ion channels along the length of a cilium from experimental current measurements.

Olfactory Signal Transduction:

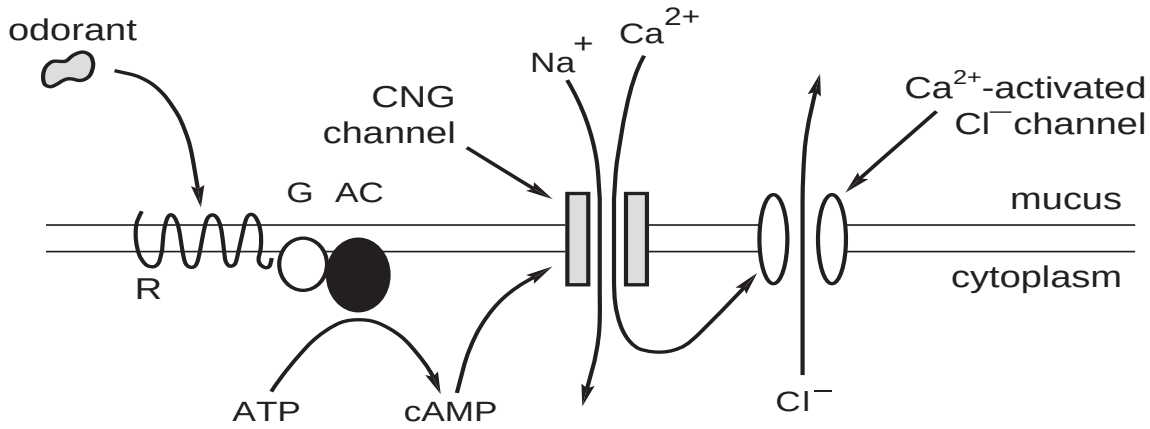


Receptor Neuron:



Steps in Signal Transduction:

Ion Channel Activity in the Ciliary Membrane.



Odorous molecule binds to G-protein-coupled receptor resulting in formation of cAMP.

cAMP activates CNG channels allowing an influx of Ca^{2+} and Na^+.

Ca^{2+} activates Cl(Ca) channels allowing an efflux of Cl^- enhancing the electrical signal.

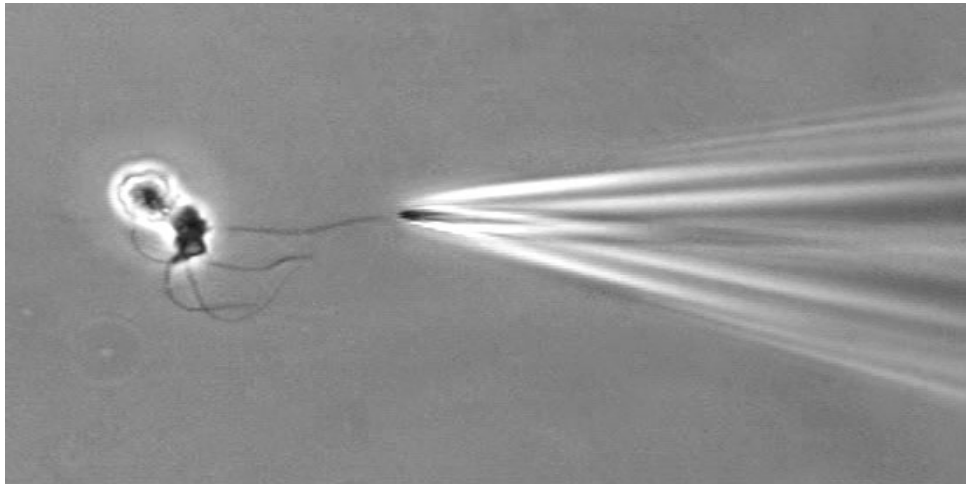
Arrangement of Channel Types:

What are the spatial distributions of CNG and Cl(Ca) channels along the length of a cilium?

Are they uniform as is often assumed?

Experimental Procedure:

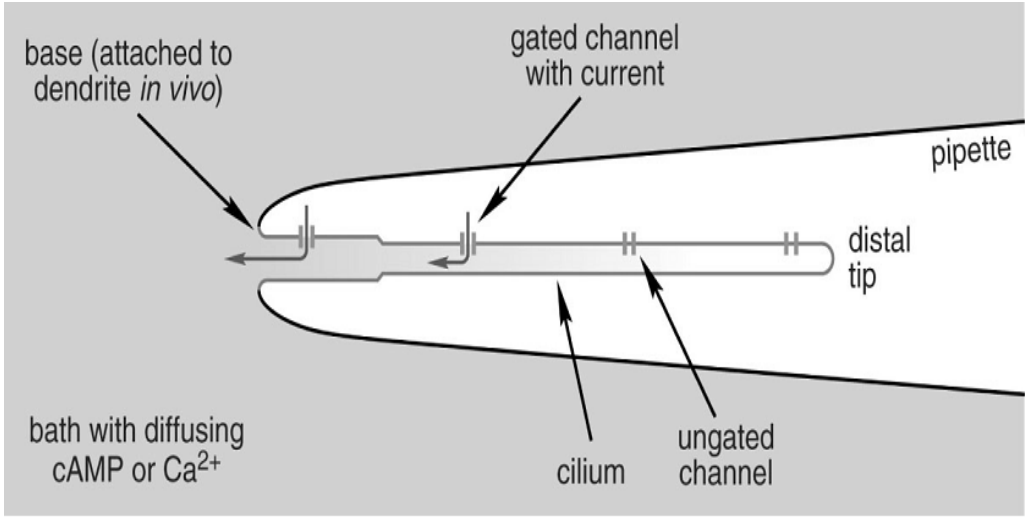
Isolate olfactory receptor neurons and remove cilia with pipette.

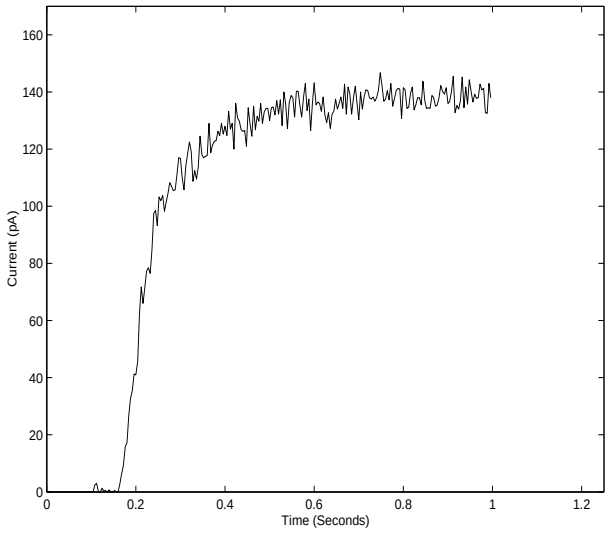


Immunocytochemistry: Difficult qualitative approach due small size of cilia (No known antibodies for Cl(Ca) channels).

CNG Channel Experiments: Exterior of cilium (inside pipette) has Na^+ solution with no Ca^{2+}. cAMP (outside pipette) diffuses into cilia activating CNG channels. Global current I across cilium membrane due to influx of Na^+ is recorded.

Cl(Ca) Channel Experiments: Interior of cilium has Cl^- solution with no cAMP. Ca^{2+} (outside pipette) diffuses into cilia activating Cl(Ca) channels. Global current I across cilium membrane due to efflux of Cl^- is recorded.





Reduced Integral Equation Model:

Assume the number of CNG channels is small the binding can be neglected and cable equation for membrane potential simplified. Open end of cilium is at $x = 0$ and closed end is at $x = L$.

cAMP Concentration: $\rho(x) =$ CNG density, $c(x,t) =$ cAMP concentration;

$$\frac{\partial c}{\partial t} = D\frac{\partial^2 c}{\partial x^2}, \quad c(0,\cdot) = c_{Bulk} \text{ and } \frac{\partial c}{\partial x}(L,\cdot) = 0, \qquad c(\cdot,0) = 0.$$

Local and Global Current:

$$J(x,t) = g_{CNG}\, P\, \rho(x)\, F(c(x,t))\, v(x,t) \qquad \text{where} \qquad F(c) = \frac{c^n}{c^n + K_{1/2}^n}$$

$$I(t) = \int_0^L J(x,t)\, dx, \quad I(t) = J_0 \int_0^L \rho(x) F(c(x,t))\, dx, \quad \rho \geq 0 \text{ and } J_0 = g_{CNG} P v_{Bulk}.$$

Constants:

Diam $=$ .28 μm, $g_{CNG} = 8.3$ pS, $P = .70$, $K_{1/2} = 1.7\mu$M, $n = 1.7$, $v_{Bulk} = -40$mV,

$D = 270\mu\text{m}^2/\text{s}$, $c_{Bulk} = 40\mu$M, $J_0 \cong 0.232\, pA/ch.$

Further Simplifications => Analytical Solution

Constants: $I \sim 100$ pA and $L \cong 40\ \mu$m

Neglect no-flux BC at $x = L$ => cAMP concentation satisfies linear diffusion;

$$c(x,t) = c_{Bulk}\text{erfc}(x/(2\sqrt{Dt})).$$

Function c has level lines with $x^2 \sim Dt$. Simplification of Hill Function: (Assume n is large)

$$F(c(x,t)) = \frac{c(x,t)^n}{c(x,t)^n + K_{1/2}^n} \cong H(c(x,t) - K_{1/2}) = H(\beta^2 t - x^2) \text{ where } \beta \sim \sqrt{D}.$$

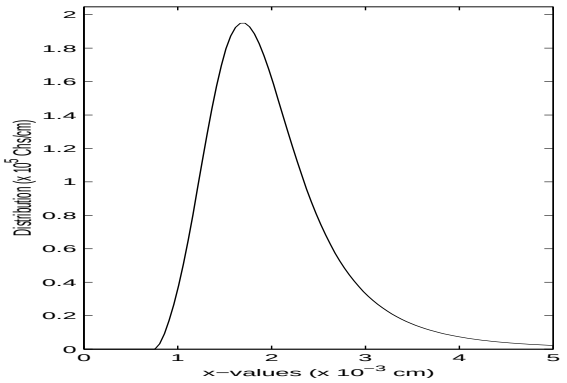
$$=> \quad I(t) = J_0 \int_0^L \rho(x) H(\beta^2 t - x^2)\, dx = J_0 \int_0^{\beta\sqrt{t}} \rho(x)\, dx \qquad (H(s) = \begin{cases} 1 \text{ for } s \geq 0, \\ 0 \text{ for } s < 0, \end{cases})$$

$$=> \quad I'(t) = \frac{1}{2} J_0 \beta t^{-1/2} \rho(\beta\sqrt{t}) \quad => \quad \rho(y) = \frac{2I'((y/\beta)^2)y}{J_0\beta^2} \quad \text{(assuming } \rho(0) = 0, \text{ and } y = \beta\sqrt{t}).$$

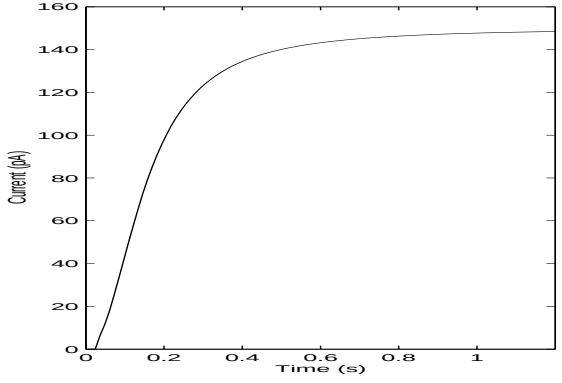
Result – Current Profile Representative of Data:

$$I(t) = \begin{cases} 0 & \text{for } 0 < t < t_{Delay} \\ I_{Max}(t - t_{Delay})^{n_I} / \left[K_I^{n_I} + (t - t_{Delay})^{n_I} \right] & \text{for } t > t_{Delay} \end{cases}$$

Distribution $\rho(x)$



Current $I(t)$



Front Tracking Algorithm (On Reduced Integral Equation Model):

Compute ρ sequentially as the ligand enters the cilium with "Wavefront" $K(x,t) = F(c(x,t))$

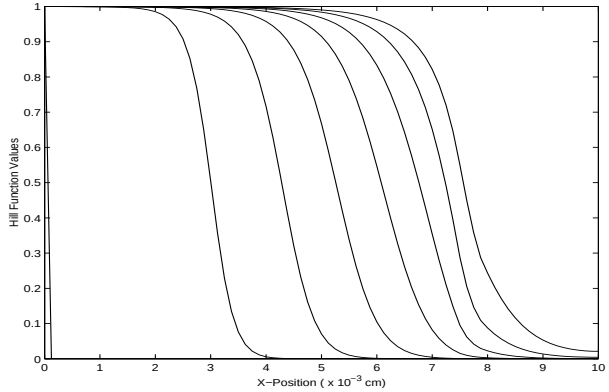
Given: $\epsilon > 0$ and $N \in \mathbf{Z}_+$ define T so $K(L,T) = \epsilon$.

Partition: $0 < t_1 < \ldots < t_N = T, \quad t_j = j\frac{T}{N}$.

Wavefront points: x_j where $K(x_j, t_j) = \epsilon$.

Approximation of ρ: $\rho^A(x) = \rho_j^A$ for $x \in [x_{j-1}, x_j]$.

Sequential determination of ρ^A (Drop $O(\epsilon)$ terms):



$$I(t_1) \cong J_0 \int_0^{x_1} K(\cdot, t_1)\rho_1^A \, dx \quad => \quad \rho_1^A = \frac{I(t_1)}{J_0 \int_0^{x_1} K(\cdot, t_1) dx}.$$

For $j = 2, \ldots, N$.

$$I(t_j) \cong J_0 \int_0^{x_{j-1}} K(\cdot, t_j)\rho^A \, dx + J_0\rho_j^A \int_{x_{j-1}}^{x_j} K(\cdot, t_j) \, dx => \quad \rho_j^A = \frac{I(t_j) - J_0 \int_0^{x_{j-1}} K(\cdot, t_j)\rho^A dx}{J_0 \int_{x_{j-1}}^{x_j} K(\cdot, t_j) dx}.$$

A Posteriori Analysis: .

Assume: $0 \le \rho^A(x) \le M$, $C_1 = \max_t |I'(t)|$ and $C_2 = \max_{(x,t)} |\partial K/\partial t|$ $(0 < t < T)$.

$$\begin{aligned} |I(t_i) \quad - \quad & J_0 \int_0^L \rho^A K(\cdot, t_i)\, dx| \\ \le \quad & \left| I(t_i) - J_0 \int_0^{x_{i-1}} \rho^A K(\cdot, t_i)\, dx - \rho_i^A J_0 \int_{x_{i-1}}^{x_i} K(\cdot, t_i)\, dx \right| + J_0 \int_{x_i}^L |\rho^A||K(\cdot, t_i)|\, dx \\ \le \quad & 0 \ + \ J_0 M L \epsilon. \end{aligned}$$

and

$$\begin{aligned} |I(t) \quad - \quad & J_0 \int_0^L \rho^A K(\cdot, t)\, dx| \\ \le \quad & |I(t) - I(t_i)| + |I(t_i) - J_0 \int_0^L \rho^A K(\cdot, t_i)\, dx| + |J_0 \int_0^L \rho^A (K(\cdot, t_i) - K(\cdot, t))\, dx| \\ \le \quad & C_1 \frac{T}{N} \ + \ J_0 M L \epsilon \ + \ J_0 M L C_2 \frac{T}{N}. \end{aligned}$$

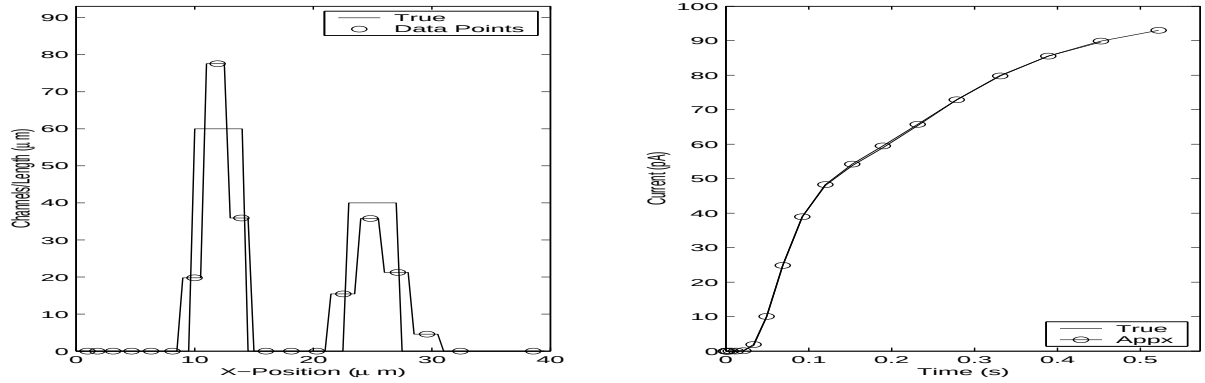
So

$$|I(t) - J_0 \int_0^L \rho^A K(\cdot, t)\, dx| \le (C_1 + J_0 M L C_2)\frac{T}{N} + J_0 L M \epsilon \ \ \le C(1/N + \epsilon).$$

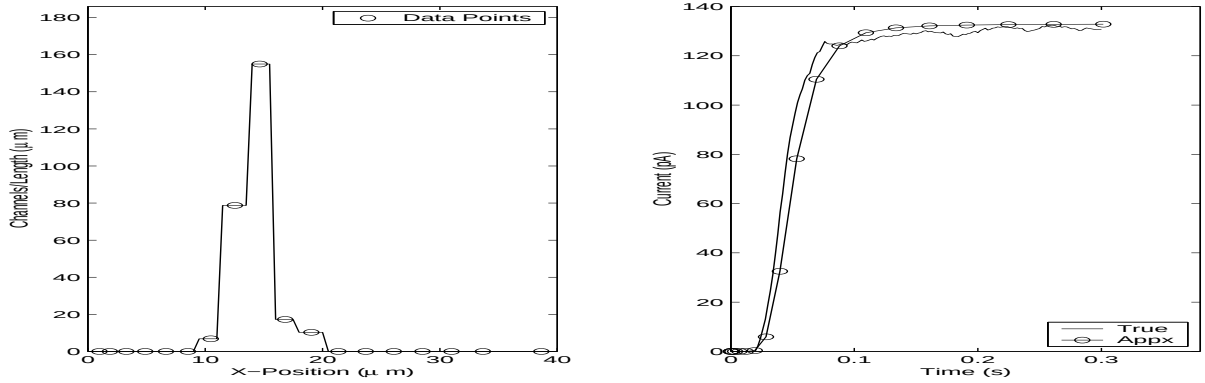
(C depends on M, J_0, L, C_1, C_2 and T.)

Sample Computations: Gauss-Seidel iterations with variable t-grid. Explicit enforcement of $\rho^A \geq 0$. Condition Numbers ($\sim 10^4$).

Simulated Data:



Laboratory Data:



Overall Results from CNG Channel Study: There were 42 experiments with 13 cilia. The CNG ion channels were typically clustered in a **narrow band roughly 10-15 μm wide.** These densities were averaged and the distance from the base of the cilium to the peak of this overall distribution was **28% of the length**. There were 1967 ± 392 CNG channels per cilium.

Overall Results from Cl(Ca) Channel Study: There were 239 experiments from 59 different cilia. Typically the Cl(Ca) ion channels were clustered in a narrow band around 5-15 μm wide. On average, the channels were concentrated a distance of 28% of ciliary length from the base. There were 4040 ± 260 Cl(Ca) channels per cilium.

Selected Papers:

1. DF, R. Flannery, C.W. Groetsch, W.B. Krantz, and S.J. Kleene, Numerical approximation of solutions of a nonlinear inverse problem arising in olfaction experimentation, *Mathematical and Computer Modelling*, **43** (2006), 945-956.

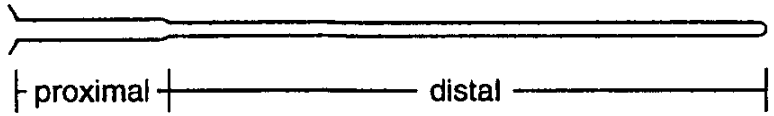
2. R. Flannery, DF and S.J. Kleene, Clustering of cyclic-nucleotide-gated channels in olfactory cilia, *Biophys. J.*, **72** (2006), 179-188.

3. D. Badamdorj, DF, and SJ Kleene, Identification of Cl(Ca) Ion Channel Distributions *PLoS ONE* **5** (2010) (12): e15676.

Future Directions:

Refinement of Models:

1. Include radial variation that changes at transition from proximal to distal ?



Use Fick-Jacobs model or ones developed in Berezhkovskii et al (2009) or Kalinay and Percus (2010).

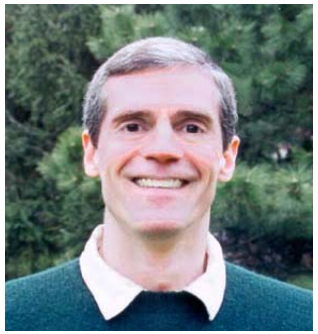
2. Develop analysis of Tikhonov Regularization approach.

National Science Foundation: (IGMS NSF DMS 0207145) (DF, 2002-4) (Cost-sharing with the Taft Foundation, Department of Mathematical Sciences, Dean of Arts and Sciences, and the Provost at the University of Cincinnati). NSF DMS 0515989 Research Grant (DF and S. Kleene, 2005-8).

National Institutes of Health: National Research Service Award (R. Flannery). National Institute on Deafness and Other Communication Disorders (R01, S. Kleene).

Mathematical Biosciences Institute.

Collaborators:



S. Kleene

Neuroscience

C. Groetsch

The Citadel

D. Badamdorj

Delaware

D. Edwards

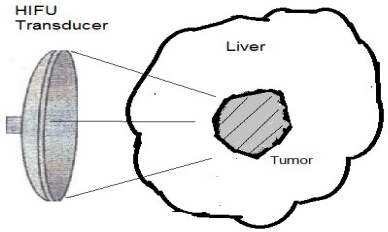
Delaware

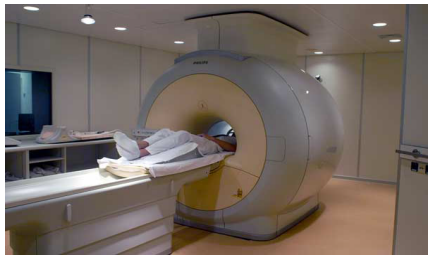
R. Flannery

NIH

(Also thanks to W.B. Krantz (Chemical Engineering – Now in Singapore)).

MRI assisted HIFU





Ultasound transducers inflict small temperature changes in tissue over region Ω that is monitored by MR imaging. Accurate solution of the inverse problem provides tissue property data used in HIFU tumor ablation.

$$\textbf{Pressure:} \begin{cases} \nabla \cdot ((1/\rho)\nabla p) + (k^2/\rho)p = 0 \text{ in } \Omega \\ \text{BC } \partial p/\partial \nu = i2\pi f \rho v_n \text{ on } \Gamma_U \text{ and } \partial p/\partial \nu = 0 \text{ on } \partial\Omega - \Gamma_U. \end{cases}$$

(ρ density, $k = 2\pi f/c + i\alpha$, f frequency, c speed of light, α absorption, v_n transducer speed.)

$$\textbf{Temperature:} \begin{cases} \rho C_T(\partial T/\partial t) = \nabla \cdot (\kappa \nabla T) - \beta(T - T_A) + Q \\ IC \;\; T(\cdot, 0) = T_A \quad \& \;\; BC \;\; T = T_A \text{ on } \partial\Omega. \end{cases}$$

(C_T specific heat, T_A ambient temperature, κ conductivity, β perfusion, $Q = \alpha|p|^2/(c\rho)$.)

Parameter Identification: Given: $T(x_j, y_j, t_\ell)$ where $(x_j, y_j) \in \Omega$. Determine α, ρ, β and κ.

Special Details − Challenges: Unknown parameter functions are piecewise constant. Solutions of Helmholtz involve high frequencies with discontinuous coefficients.

Beginnings/Theory for Simplified Heat Conduction:
Consider:

$$-U'' + \beta U = f \quad \text{with boundary conditions} \quad U(0) = U(1) = 0.$$

where **unknown** is

$$\beta(x) = \begin{cases} \beta_0 \text{ for } 0 \le x \le m, \\ \beta_1 \text{ for } m < x \le 1, \end{cases} \qquad 0 < m < 1, \quad m = O(1)$$

Given: Piecewise linear data function U_D defined on a partition of $\Omega = [0, 1]$ with subintervals of uniform width h_D.
Assume there is a solution $U = U(x)$ associated with β and

$$\|U - U_D\| \le \epsilon \qquad (0 < \epsilon << 1).$$

Inverse Problem Solver:
Use smooth cutoff functions $\omega_0 \in C_0^\infty(0, m)$ and $\omega_1 \in C_0^\infty(m, 1)$.
Approximation β^A:

$$\beta_0^A = \frac{\int_\Omega f\omega_0 \, dx + \int_\Omega U_D\omega_0'' \, dx}{\int_\Omega U_D\omega_0 \, dx} \quad \text{and} \quad \beta_1^A = \frac{\int_\Omega f\omega_1 \, dx + \int_\Omega U_D\omega_1'' \, dx}{\int_\Omega U_D\omega_1 \, dx}.$$

Theorem: There exists a constant C independent of ϵ and h_D such that

$$\max\{|\beta_0 - \beta_0^A|, |\beta_1 - \beta_1^A|\} \le C\epsilon.$$

Challenges/Directions:

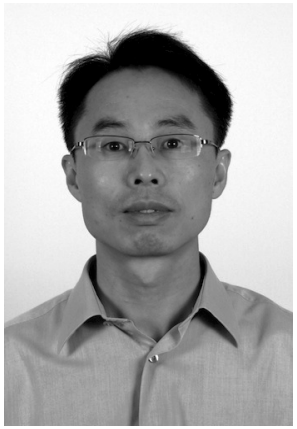
(i) Output Least Squares Approach – Avoid assumption of existence of U to U_D.

(ii) Impact of new, first set, of data from Yu Li's lab ?

(iii) XFEM for Helmholtz – "X" for high frequencies ?

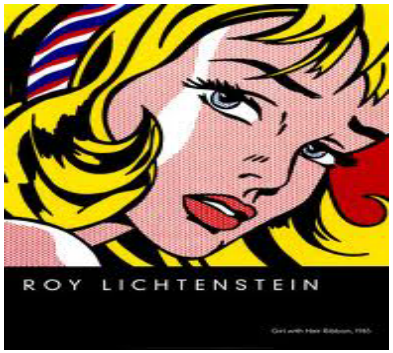
The HIFU "Lab":

DF



Yu Li

Benjamin Vaughan Jr.



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Mathematical Sciences

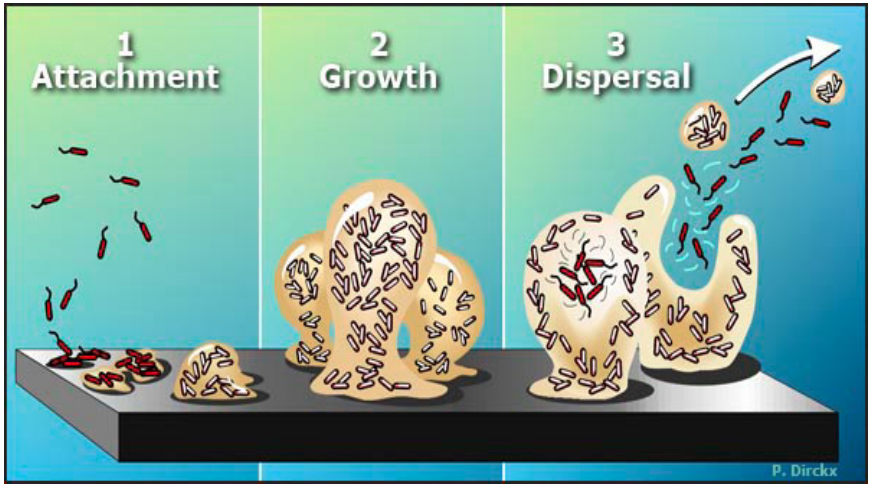
Inverse Problems Involving Models of Biofilms in Urban Pipes

The natural or deliberate release of a pathogen into urban water pipes can have a profound effect on the quality of water used for human consumption. Biofilms can trap the dangerous pathogens, enhance their growth and release them at a later time.

Gap: *No recent models involving biofilms simulate attachment, very few handle detachment and none consider high (or modest) Reynolds number flows and/or the onset of turbulence.*

Specific Objectives:

1. Quantify **attachment and detachment** of pathogens to biofilms.
2. Develop biofilm/fluid models in **urban pipes** (Diameter $\sim$ 10 cm) with rough surfaces.
3. Take incremental steps toward high Reynolds Number/Turbulent Regimes.



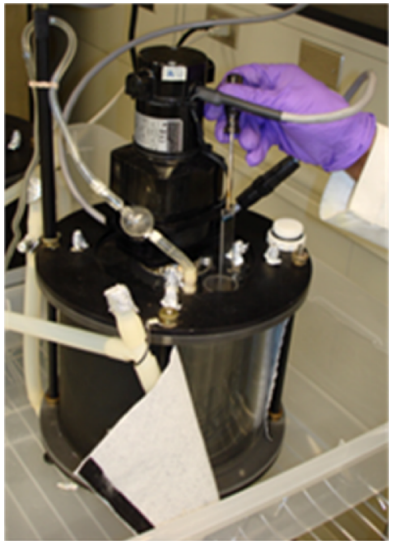
Colonies of Bacteria that form on solid surfaces are called biofilms.

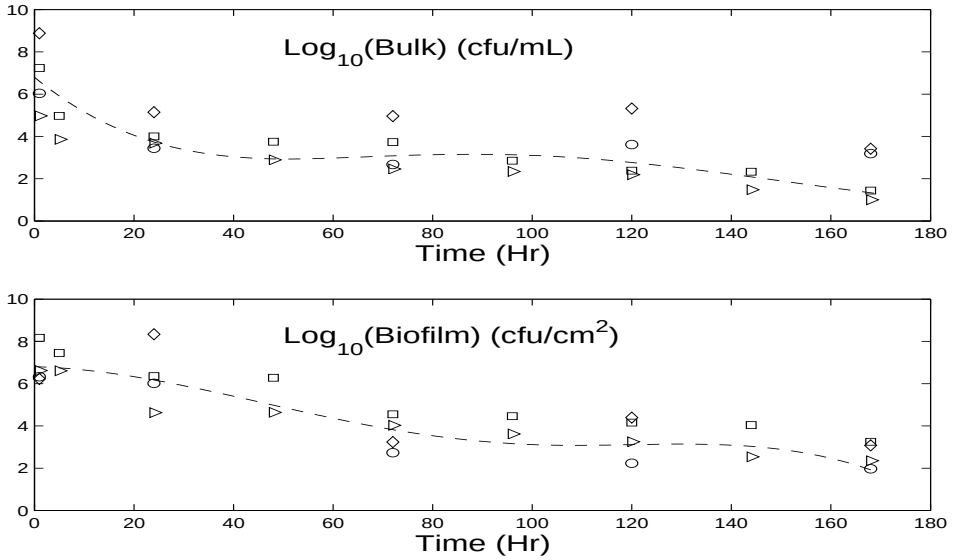
Biofilms are present in tooth decay, remediation of wastewater, maintenance of navy ships, transmission of bacteria in hospital tubing and cystic fibrosis.

Extracellular Polymeric Substance (EPS) is a substance produced by biofilm bacteria that enhances their colony/structure.

Other Players: Disinfectants (Chlorine, bacteria very tolerant in biofilm), Nutrients (Aerobic and Anaerobic), Fluid Dynamics (Erosion and Sloughing, Shear Stress, Fast vs Slow).

Annular Reactor Modeling:





Experiment: Pathogens are "spiked" into an AR with a fully developed biofilm; the level of pathogens in bulk and biofilm is tracked over time (Constant inflow and outflow).

Basic ODE Model:
Following Bakke et al (1984) and Jones et al (2003):

$$\frac{dx_f}{dt} = -\alpha x_f + \beta \frac{S_A}{V} x_b - \frac{Q}{V} x_f \qquad \text{and} \qquad \frac{dx_b}{dt} = \alpha \frac{V}{S_A} x_f - \beta x_b$$

Identification Problem: Given data on concentration in bulk fluid, $x_f = x_f(t)$ and biofilm $x_b = x_b(t)$ find parameters α and β.

Output Least Squares Approach: Given data Y_D find parameter $\vec{p}$ so there is y that satisfies

$$dY/dt = f(y, \vec{p}) \qquad \text{with} \qquad y(0) = Y_0 \quad \text{on} \quad [0, T].$$

Use minimization search (e.g. MATLAB *fminsearch*) to find $y \cong Y_D$ and $\vec{p^*}$ that minimizes

$$J(\vec{p}) = \frac{1}{2} \| Y_D - y(\cdot; \vec{p}) \|_{L^2(0,T)}$$

where $y(\cdot; \vec{p})$ satisfies the IVP

$$dy/dt = f(y, p) \qquad \text{with} \quad y\Big|_{t=0} = Y_0$$

Biofilm Model Specifics:
The approximation process involves the N data points $(t_1, \widehat{x}_f(t_1)), \ldots, (t_N, \widehat{x}_f(t_N))$ for fluid concentrations and $(t_1, \widehat{x}_b(t_1)), \ldots, (t_N, \widehat{x}_b(t_N))$ for the biofilm. Weighted Minimization functional was

$$E_W(\alpha, \beta, k_f)^2 = \sum_{i=1}^{N} w_i^{(b)} [\log_{10}(\widehat{x}_b(t_i)) - \log_{10}(x_b(t_i; \alpha, \beta))]^2 + \sum_{i=1}^{N} w_i^{(f)} [\log_{10}(\widehat{x}_f(t_i)) - \log_{10}(x_f(t_i; \alpha, \beta))]^2$$

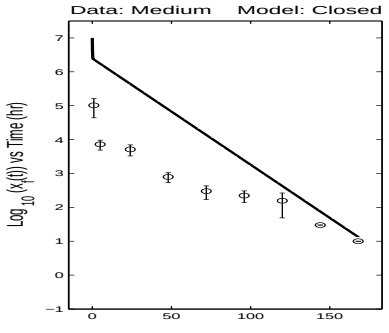
with, for $i = 1, \ldots, N$,

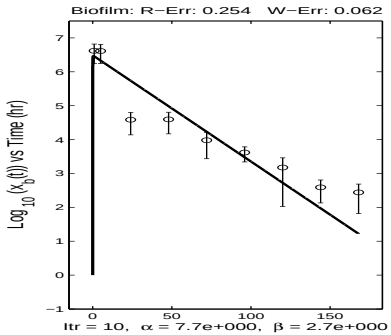
$$w_i^{(b)} = \frac{x_b(t_i)}{\sigma_i^{(b)}\ \Phi_b}, \quad w_i^{(f)} = \frac{x_f(t_i)}{\sigma_i^{(f)}\ \Phi_f}, \quad \Phi_b = \sum_{i=1}^{N} \frac{x_b(t_i)}{\sigma_i^{(b)}} \quad \text{and} \quad \Phi_f = \sum_{i=1}^{N} \frac{x_f(t_i)}{\sigma_i^{(f)}}.$$

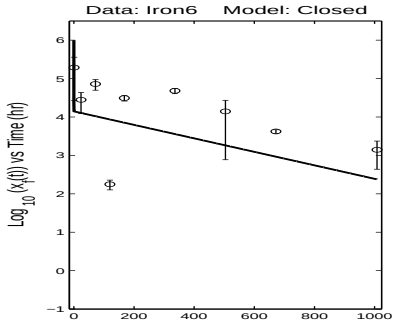
Especially interested in *relative error*;

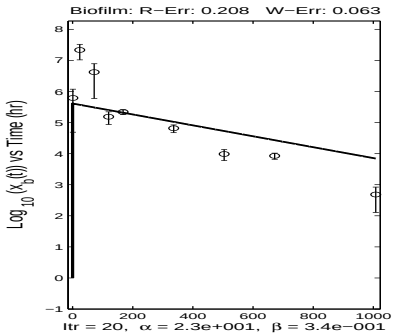
$$R(\alpha, \beta) = \frac{J(\alpha, \beta)}{D} \quad \text{where} \quad D^2 = \sum_{i=1}^{N} [\log_{10}(\widehat{x}_f(t_i))]^2 + \sum_{i=1}^{N} [\log_{10}(\widehat{x}_b(t_i))]^2.$$

Output Least Squares Results:









Data	α	β	Relative Error	Weighted Error
Polycarbonate	7.7	2.7	0.254	0.062
Iron	23	0.34	0.208	0.063

Other Steps for Simple ODE Model:

New DE Model with Linear Decay $k_f x_f$ for Bulk Pathogen Equation.

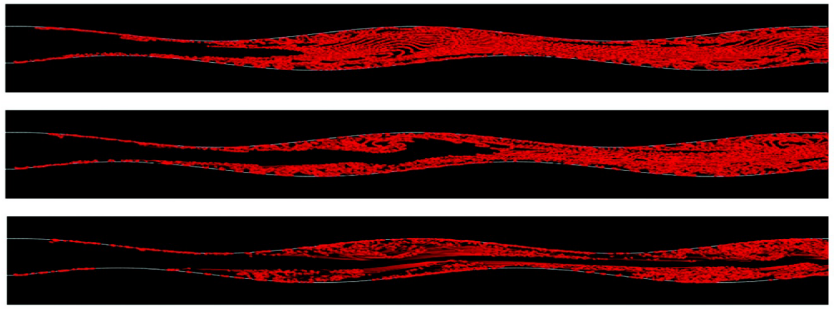
Linear Regression on Closed Form Solutions of DE Models.

Contour Plots, Error vs (α, β), reveal robust solutions in ratio β/α.

Next Steps/Directions:

Biofilm Model: Wanner-Gujer, Multi-species (N. Cogan) etc. (Neglect influence of thin biofilm on flow.)

Rough Pipe Simulations:
Immersed Boundary Method
(Sookkyung Lim)



Turbulent flow by $k-\epsilon$ Reynolds Averaged Navier-Stokes (RANS) method (B. Vaughan).

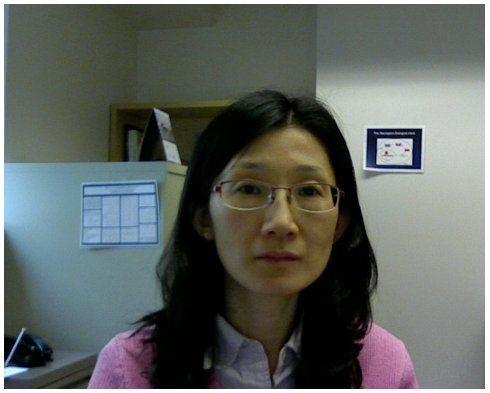
Improved Data Collection – Dyed Tracer Organisms.

Simulation of Pathogen and Biofilm in Rivers Persistance – Delivery – Evolution (with D. Hassett).

Seeking funding from NSF Environmental Engineering with proposal entitled *Mathematical Modeling of Biofilms in Urban Pipes and the Spread of Dangerous Pathogens* (PI Vaughan & Co-I's Kupferle (Engr), D.F. and Lim).

The Biofilm "Lab":

M. Kupferle



Sookkyung Lim

D.F.

Nick Cogan (FSU)

Benjamin Vaughan Jr.

Dan Hassett