Lecture of BCB 570 Spring 2013
Mathematical modeling and study of chemotaxis processes

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OUTLINE

INTRODUCTION

- Taxis (ancient Greek$\tau\acute{\alpha}\xi\iota\zeta$: arrangement) is an innate response by organisms to directional stimulus or gradient of stimulus intensity.
  - Aerotaxis, energy-taxis, phototaxis, gravitaxis, thermotaxis, chemotaxis, etc.

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- Chemotaxis is a type of taxis, whereby single-cells or multicellular organisms direct their movement according to certain chemicals in their environment.
- Examples of chemotaxis
  - Bacteria swim toward the highest concentration of glucose;
  - Immune cells toward infection sites with higher concentration of chemokines (e.g. Mϕ attracted by INF-γ);
  - Sperms move toward the egg during fertilization;
  - *E.coli* swims away from inorganic salts.

HISTORY FROM BIOLOGY

- Migration of cells in culture-A.P. van Leeuwenkoek (1703)
- Chemotaxis in bacteria-T.W. Engelmann (1881) and W.F.Pfeffer (1884)
- Chemotaxis in ciliates-H.S. Jennings (1906)
- Chemotaxis in immune response: phagocytosis-E.Metchnikoff (1908)
- Fundamental definition of chemotaxis-given in 1930s
- Explosion of research results since 60s-70s- E.g. J. Adler on signal transduction (1973)

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- Regulation mechanism of bacteria chemotaxis is known (Cluzel, Surette and Leibler 2000), while mechanism of eukaryotic cell chemotaxis is not conclusive yet.
- There exists different types of chemotaxis depending on the sources of chemicals: Chemokinesis, haptotaxis and necrotaxis

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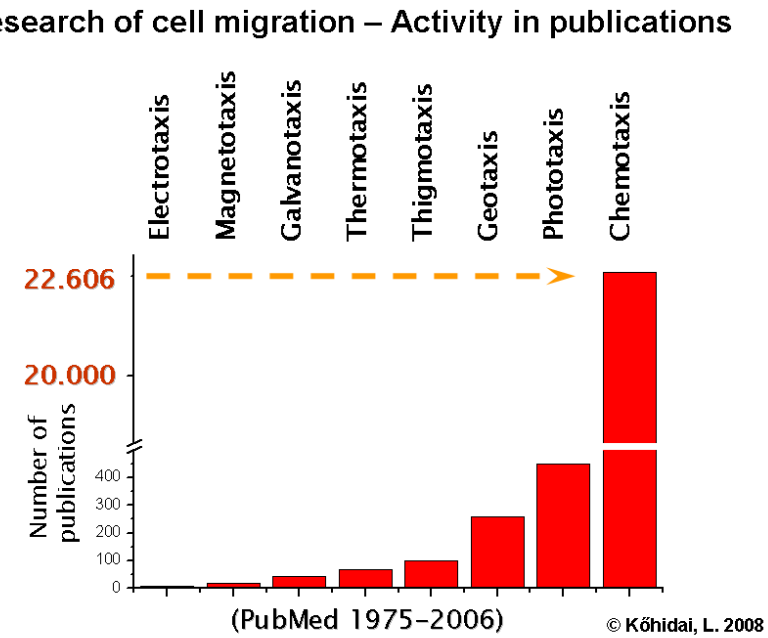
- Chemotaxis process has drawn great attentions in research.



- Movie: https://www.youtube.com/watch?v=EpC6G_DGqkI

MATHEMATICAL APPROACH

- Mathematical modelings of chemotaxis focus on bio-mechanics or physical movement rather than biochemistry part.
- The biological system under consideration is NOT "well-mixed", mathematically it is not spatially homogeneous, i.e. there exists a distribution of quantity of interest on spatial domain (may or may not evolve along time).

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- The spatial heterogeneity arises in many biological systems across different scales and different processes: e.g. gene expression, protein dynamics, cellular interactions, wound healing, ecological dynamics, population evolution etc.

MATHEMATICAL APPROACH

- Spatially heterogenous system is usually modeled by partial differential equations (PDEs), which models mechanism involving changes of rate with respect to more than one variable.
- Modeling system by partial differential equations usually involves derivative w.r.t. time (evolution) and derivatives w.r.t. space (distribution), but may also involves derivatives w.r.t. other variables such as age (in structure equations).

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- PDE models can be derived from interacting particle systems using techniques like hydrodynamical limits, and they are more likely derived from known physical mechanism (modeled by spatial movement) and biological mechanism (modeled by interactions).

MATHEMATICAL APPROACH

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  - Questions on time scale may determine whether we need PDE models or simply ODE models;
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  - Also need to consider physical domain (bounded, unbounded), boundary conditions (Dirichlet, Neumann, Robbins, Free boundary etc).
- PDE models (even ODE model) in general provide modeling of the mean structure and do not take into account the variation from data. From this point of view, it has no difference than linear model in statistics.

MODELING CHEMOTAXIS

- Chemotaxis process is spatial heterogeneous and biological system involved evolve along time.
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  - e.g time spend for cell movement is not too large or too small compare to cell's double life.
- There might exist multiple scales for some system involving chemotaxis.
- Chemotaxis process, in the language of applied mathematics, is a reaction-convection-diffusion process.
- Reaction-convection-diffusion process is a physical phenomenon where particles, energy or any quantities transferring inside physical system due to diffusion and convection processes, and also reacting with the system or themselves.

MODELING REACTION-CONVECTION-DIFFUSION

- Assume $u(x,t)$ is some physical quantity of interest like concentration in mass transfer, temperature for heat conduction etc.
- The temporal dynamics of u is governed continuity assumption:

the rate of change for a scalar quantity in a differential control volume is given by flow and diffusion into and out of that part of the system along with any generation or consumption inside the control volume

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- This law is summarized as

$$\frac{\partial u}{\partial t} + \nabla \cdot \vec{J} = s$$

where $\vec{J}$ is the total flux and s is the net volumetric source for u.

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- Total flux is $-D\nabla u + \vec{v}u$ so that the modeling PDE is

$$\frac{\partial u}{\partial t} + \nabla \cdot (-D\nabla u + \vec{v}u) = s(u).$$

MODELING CHEMOTAXIS PROCESS

- The modeling equation is also called Smoluchowski equation or continuity equation, it is the
  - Maxwell's equations in electromagnetic theory; continuity law in elasticity, Navier-Stokes's equations in fluid mechanics; the conservation law in thermodynamics; Schrödinger equation in quantum mechanics; tensor equation in general relativity, etc.

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- Physically, we also need biologically sensible boundary condition of u.

KELLER SEGEL MODEL

- **Keller-Segel Equations** is the fundamental equation modeling chemotaxis (Keller and Segel, 1970):

  Denote $u(x,t)$ the population of cells, $v(x,t)$ the concentration of chemoattractant, $\eta(x,t)$ the concentration of complex of enzyme and chemoattractant, and $p(x,t)$ the concentration of enzyme

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- $$\begin{cases} u_t = \nabla(k_1(u,v)\nabla u - k_2(u,v)\nabla v) \\ v_t = k_c\Delta v - r_1 vp + r_{-1}\eta + uf(v) \\ p_t = k_p\Delta p - r_1 vp + (r_{-1}+r_2)\eta + ug(v,p) \\ \eta_t = k_\eta\Delta\eta + r_1 vp - (r_{-1}+r_2)\eta. \end{cases} \tag{1}$$

  for $(x,t) \in \Omega \times \mathbb{R}^+$. Ω is a **bdd domain** in $\mathbb{R}^N$ with $N \leq 3$.

KELLER-SEGEL EQUATIONS

The famous Keller Segel Equations, K-S equations, is a simplified version of (1) based on assumptions:

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KS EQUATION (ALSO KNOWN AS CHEMOTAXIS EQUATION)

$$\begin{cases} u_t = \nabla(k_1(u,v)\nabla u - k_2(u,v)\nabla v) \\ v_t = k_c\Delta v - k_3(v)v + uf(v) \\ \frac{\partial u}{\partial n}\Big|_{\partial\Omega} = \frac{\partial v}{\partial n}\Big|_{\partial\Omega} = 0 \\ u(x,0) = u_0,\ \ v(x,0) = v_0. \end{cases} \tag{2}$$

JAGER-LUCKHAUS EQUATION

- Using conservation of mass and transform $v := v - v_\Omega$, Jager and Luckhaus (1989) introduced

$$\begin{cases} u_t = \nabla(\nabla u - \chi u \nabla v) \\ \frac{1}{k_c}(v_t + \gamma v) = \Delta v + \beta(u - u_\Omega). \end{cases} \tag{3}$$

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- By assuming $k_c \gg 1$ and rescaling upon the average of u, the **J-L equation** is given as $(v := v/(\beta u_\Omega),\ u := u/u_\Omega)$

$$\begin{cases} u_t = \nabla(\nabla u - \chi u \nabla v) \\ 0 = \Delta v + (u - 1). \end{cases} \tag{4}$$

OTHER MAJOR VARIANT EQUATIONS

- Assuming the chemoattractant quickly reaches the stationary state, T. Nagai (1994) present

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- Similar chemotaxis type systems were proposed such as the angiogenesis equation for vasculature growth (Levine and Sleeman 1997):

$$\begin{cases} u_t = \nabla(\nabla u - \chi(v) u \nabla v) \\ v_t = -v^m u \end{cases},$$

$m > 0$, χ is positive and decreasing on $\mathbb{R}^+$.

THEORETICAL STUDY OF PDE MODEL

- In general, theoretical study of PDE model starts from answering questions
  - Does the proposed PDE model have solution for a small amount of time (local existence)? Does the solution exists for all time (global existence)?
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- How does the proposed model react to small perturbation of the initial condition or boundary condition?
- Asymptotically, what does the solution look like? Is the system sensitive to any particular parameter?

NANJUDIAH CONJECTURE

Definition (Blow up solution to (2)): Let u, v be the solution of (2) for the corresponding initial data. The solution blows up if $||u(\cdot,t)||_{L^\infty}$ or $||v(\cdot,t)||_{L^\infty}$ becomes unbounded in either finite or infinite time, i.e. $\exists\ T_{max} \in (0,\infty]$ s.t.

$$\lim_{t\to T_{max}} \sup ||u(\cdot,t)||_{L^\infty} = \infty, \ \textit{or} \ \lim_{t\to T_{max}} \sup ||v(\cdot,t)||_{L^\infty} = \infty.$$

Nanjudiah Conjecture (1973): Aggregation, happening in finite time, is such that the cells are distributed in the form of $\delta-$function concentrations.

CHILDRESS-PERCUS CONJECTURE

Definition (chemotactic collapse by Childress-Percus): The chemotactic collapse occurs if the cell density form a $\delta-$function at the end.

Childress-Percus Conjecture (1981): For simplified (most popular) K-S equation

$$\begin{cases} u_t = \nabla(\nabla u - \chi u \nabla v) \\ v_t = k_c \Delta v - \gamma v + \alpha u \end{cases} \tag{6}$$

(i) Collapse or blow up can not occur in one-dimensional space;
(ii) "May or May not be in two dimensions", depending on the cell population (initial population);
(iii) Must happen in three or more dimension

BLOW UP OF SOLUTION–EARLY RESULTS

- **Jager-Luckhaus theorem (1992):** Let Ω be a disk. There exists a positive number c^* such that if $\chi > c^*$ then radially symmetric positive initial data can be constructed so that explosion of u, the solution to (3), happens in the center of the disc in finite time.

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- **Nagai theorem (1995):** For the system (5), let $N \geq 2$ and define an artificial functional E_θ with respect to the N^{th} momentum

$$M_N = \frac{1}{w_N} \int_\Omega u(x,t)|x|^N.$$

If $E_\theta(M_N(0)) < 0$ (E_θ is an entropy function) then $T_{max} < \infty$ and

$$\limsup_{t \to T_{max}} ||u||_\infty = \infty.$$

AGGREGATION

- Showing blow up of the solution does not solve the conjectures completely since it does not reveal any geometric features of the blow up set.
- In weak*-topology, the solution u converges to a Radon measure as $t \to T_{max}$. It is needed to show $T_{max} < \infty$ and that limiting Radon measure is $\delta-$measure with countably many isolated supporting points.

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Nagai theorem (1995): Let $N \geq 2$, then the radially symmetric solution of (5) satisfies $u(r,t) + v(r,t) \leq K(n)$ for $\frac{1}{n} \leq r \leq L$ and $0 \leq t < T_{max}$, where $K(n) \to \infty$ as $n \to \infty$. This implies that blow-up can occur only at point $r = 0$.

AGGREGATION—HERRERO-VELAZQUEZ'S THEOREM

Herrero-Velazquez theorem (1996,1997): Let $\Omega \subset \mathbb{R}^2$ be the open ball with radius $R > 0$. Then for sufficiently small $T > 0$, there exists radial solution of problem under consideration, (6) which blows up at $r = 0$ and $t = T$, such that

$$u(r,t) \to \frac{8\pi}{\chi}\delta + f(r) \text{ as } t \to T$$

in the sense of measure, where δ is the Dirac measure centered at $r = 0$, and

$$f(r) = \frac{C}{r^2} e^{-2|\log r|^{1/2}}(1 + o(1))$$

as $r \to 0$ where C is a constant depending on χ, Γ.

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- For $N = 1$, global existence is obtained.
- For $N = 2$,
  - For radially symmetric case, aggregation is obtained.
  - For non-radially symmetric case,
    - If $||u_0||_1 = 4\pi$, aggregation is true and concentrate toward the boundary (single point);
    - If $4\pi < ||u_0||_1 < 8\pi$, blow up is true and the blow up set toward the boundary, however, aggregation is NOT clear;
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    - If $||u_0||_1 > 8\pi$, blow up is true but no information about aggregation is available.
- For $N = 3$, the only known results is for (3), Herrero and Velazquez obtain formal expansion to show the blow up. No aggregation results for either radial symmetric or non-radial symmetric.

HOW TO STUDY KS EQUATION?

- Theoretical study reveals a lot of interesting mathematical and biological conclusions.
- Numerical simulation of PDE system provide an alternative approach to understanding chemotaxis process based on KS equations. It provides *in silico* experiments on large system made from chemotaxis processes. This is referred as Direct Problem.
- Given lab data, based on KS equation, we can estimate the parameters such as chemotaxis or diffusion rates. This is referred as Inverse Problem.

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- Central scheme and discontinuity Galerkin methods are proven to be efficient to handle large chemotaxis system lately.
- In general, chemotaxis process is competition between diffusion and aggregation, with sophisticated reaction terms, numerical scheme should honor these aspects

FINITE DIFFERENCE

- What is finite difference?
  - $f \in C^1(\mathbb{R})$ then $f'(x_0)$ can be approximated by

$$f'(x_0) = \frac{f(x_0+h)-f(x_0)}{h}, \text{ or } f'(x_0) = \frac{f(x_0)-f(x_0-h)}{h}$$

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  - Forward/backward difference v.s. central difference: $O(h)$ v.s. $O(h^2)$, and stable v.s. oscillatory
- Extend this to $\partial_t u$, $\partial_x u$ and even Δu for differentiable u.

FINITE DIFFERENCE APPROACH TO DIFFUSION EQUATION

- The second equation in KS equation is called diffusion equation

$$\partial_t c = D\Delta c + \beta u - \alpha c, \text{or}$$

$$\partial_t c = \nabla \cdot (D(c,u)\nabla c) + \beta u - \alpha c.$$

- What is the difference between the two equations?

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$$\partial_t c = D\Delta c + \beta u - \alpha c, \text{or}$$

$$\partial_t c = \nabla \cdot (D(c,u)\nabla c) + \beta u - \alpha c.$$

- What is the difference between the two equations?
- 1-D illustration
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  - Other approaches on c_{xx}? How to solve them?
  - Difference equation is

$$\frac{c_i^{n+1} - c_i^n}{\Delta t} - \frac{1}{\Delta x^2}\left(\theta \partial_f^h c + (1-\theta)\partial_b^h c\right) = \beta u_i^n - \alpha c_i^n$$

1-D ILLUSTRATION FOR SECOND EQUATION (CONTINUE)

- For second equation
  - Let $\{x_i\}$ be a uniform partition, $x_i = i\Delta x$ and $x_{i+\frac{1}{2}} = (i+\frac{1}{2})\Delta x$.
  - Let c_i^n, u_i^n denote the numerical approximation of $c(x,t), u(x,t)$ at the point (x_i, t_n).
  - Define $\Delta^+ a_i = a_{i+1} - a_i$, $\Delta^- a_i = a_i - a_{i-1}$, and $\theta = \frac{1}{2}$ or 1.

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- Define

$$\Gamma_{i-\frac{1}{2}} = D\left(\frac{c_{i-1}^n + c_i^n}{2}, \frac{u_{i-1}^n + u_i^n}{2}\right)$$
$$\approx D\left(\frac{c(x_{i-1}, t^n) + c(x_i, t^n)}{2}, \frac{u(x_{i-1}, t^n) + u(x_i, t^n)}{2}\right).$$

- If $D \equiv$ const then $\Gamma_{i-\frac{1}{2}} \equiv$ const.

1-D ILLUSTRATION FOR SECOND EQUATION (FINAL FORM)

- The finite difference of equation of c is then

$$\frac{c_i^{n+1} - c_i^n}{\Delta t} - \frac{1}{\Delta x^2}\left[\theta\Delta^+(\Gamma_{i-\frac{1}{2}}\Delta^- c_i^{n+1}) + (1-\theta)\Delta^+(\Gamma_{i-\frac{1}{2}}\Delta^- c_i^n)\right]$$
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- What about multiple dimension?

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$$=\beta u_i^n-\alpha c_i^n$$

- What about multiple dimension?
- The final form is always $Ax=b$. How to solve it? Fixed point, Gauss-Seidle, Conjugate-gradient etc. (Matrix is sparse)

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- Yes and NO.
- MUSCL scheme and operator splitting.
  - MUSCL is a finite volume method (refers to the small volume surrounding each node point on a mesh)
  - Volume integrals are converted to surface integrals (divergence theorem), they evaluated as fluxes at the surfaces of each finite volume (meshes)
  - Flux entering a given volume is identical to that leaving the adjacent volume, these methods are conservative.
  - Easily formulated to allow for unstructured meshes.
  - Used primarily in CFD.

FINITE VOLUME SCHEME

- MUSCL (Monotone Upstream-centered Schemes for Conservation Laws) provides high accuracy where the solutions exhibit shocks, discontinuities, or large gradients.
- Introduced by van Leer (1979), attempted to improve Godunov scheme (1959, "God's scheme"–S. Osher) that is first order accurate in both space, and time.

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- 1-D Illustration of FVM of $\partial_t u + \partial_x f(u) = 0$.
  - $f > 0$ means flow to the right and $f < 0$ represents flow to the left
  - Define volume average of u at x_i and t_1 as

$$\bar{u}_i(t_1) = \frac{1}{x_{i+1/2} - x_{i-1/2}} \int_{x_{i-1/2}}^{x_{i+1/2}} u(x, t_1) dx$$

  - Integration of PDE over time gives

$$u(x, t_2) = u(x, t_1) - \int_{t_1}^{t_2} f_x(x, t) dt.$$

FVM (CONTINUE)

- FVM (continue)
  - Volume average of $u(x,t)$ at time $t_2 > t_1$ is

$$\bar{u}_i(t_2) = \frac{1}{\Delta x_i} \int_{x_{i-1/2}}^{x_{i+1/2}} \left[u(x,t_1) - \int_{t_1}^{t_2} f_x \right] dx$$

  - Using divergence theorem

$$\bar{u}_i(t_2) = \bar{u}_i(t_1) - \frac{1}{\Delta x_i} \left[\int_{t_1}^{t_2} f_{i+1/2} - \int_{t_1}^{t_2} f_{i-1/2} dt \right]$$

    where $f_{i\pm 1/2} = f(u(x_{i\pm 1/2}, t))$.

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    where $f_{i\pm 1/2} = f(u(x_{i\pm 1/2}, t))$.
  - Semi-discrete scheme with cell centers indexed by i and cell edge fluxes indexed by $i \pm 1/2$ is then

$$(\bar{u}_i)_t + \frac{1}{\Delta x_i} \left[f_{i+1/2} - f_{i-1/2} \right] = 0$$

    where value for the boundary fluxes $f_{i\pm 1/2}$ can be **reconstructed** by interpolation of cell averages.

GODUNOV'S SCHEME

- Godunov's scheme
  - Discretize of above method on time giving

$$\bar{u}_i^{n+1} = \bar{u}_i^n - \frac{1}{\Delta x_i}\left[\int_{t_n}^{t_{n+1}} f_{i+1/2} - f_{i-1/2}\, dt\right]$$

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  - Godunov replaced the time integral with Forward Euler method (for integral) that

$$\bar{u}_i^{n+1} = \bar{u}_i^n - \frac{\Delta t}{\Delta x_i}\left[\hat{f}_R(\bar{u}_i^n, \bar{u}_{i+1}^n) - \hat{f}_R(\bar{u}_{i-1}^n, \bar{u}_i^n)\right]$$

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- What is $u_i^n \approx u(x_i, t^n)$ finally? $u(x_i, t^n)$ is approximated by cell average $\bar{u}_i^n$, a piecewise constant approximations for each cell.

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for any $x \in (x_i, x_{i+1}]$.

- $f_{i\pm 1/2}$ is changed to $f(u_{i\pm 1/2})$ where $u_{i+1/2} = (u_i + u_{i+1})/2$ at t_n.

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- This method provides second-order accuracy but it is not TVD (total variation diminishing) and introduce spurious oscillation at discontinuities.

1-D SIMULATION USING GODUNOV'S SCHEME AND 2ND ORDER CONSTRUCTION

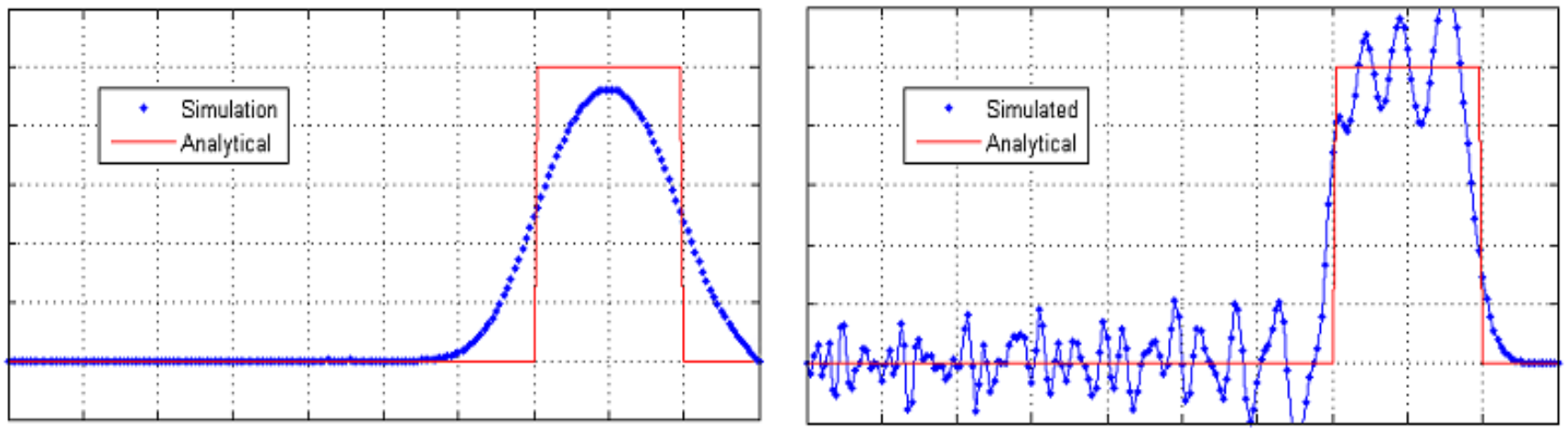

FIGURE : $u_t + u_x = 0$.

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- The key is how to approximate the flux numerically. MUSCL use nonlinear combination of first and second-order approximation to get numerical fluxed $F^*_{i\pm1/2} = F(u^*_{i\pm1/2}) = F(h^*_{i\pm1/2}(u^L_{i\pm1/2}, u^R_{i\pm1/2}))$ that $h^*_{i\pm1/2}$ represent scheme dependent functions.
- $u^L_{i+1/2} = u_i + 0.5\phi(r_i)(u_{i+1} - u_i), u^R_{i+1/2} = u_{i+1} - 0.5\phi(r_{i+1})(u_{i+2} - u_{i+1})$ and $u^L_{i-1/2} = u_{i-1} + 0.5\phi(r_{i-1})(u_i - u_{i-1}), u^R_{i-1/2} = u_i - 0.5\phi(r_i)(u_{i+1} - u_i)$, with $r_i = \frac{u_i - u_{i-1}}{u_{i+1} - u_i}$.

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- $\phi(r_i)$ is called limiter function that equals to zero when $r_i \leq 0$ and equals to 1 when $r_i = 1$. $\phi(r_i)$ is chosen in practice to guarantee TVD properties.
- MUSCL degrades to first order at local extrema, but tends to second order over smooth parts of the domain.

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NUMERICAL APPROACH TO FIRST EQUATION

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- First equation in KS equation can be approximated by the following two equations during a time step, for $t \in [0, \Delta t]$,

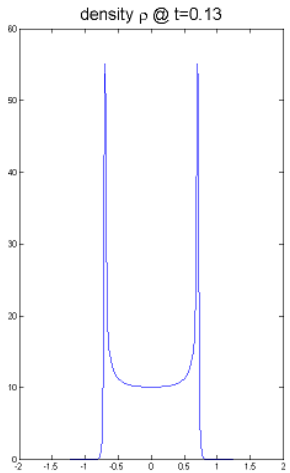
$$\widetilde{u}_t + \mathrm{div}(\chi \nabla c \widetilde{u}) = 0, \ \widetilde{u}(x,0) = \rho(x, t_n);$$

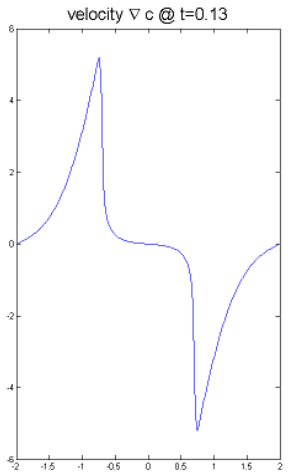
and

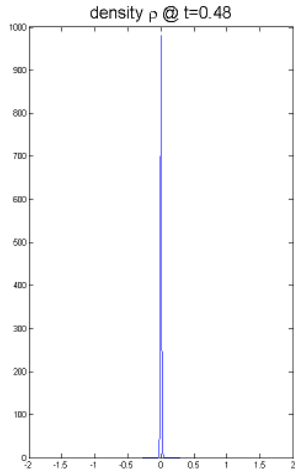
$$u_t = \mathrm{div}(\mu \nabla u), \ \left.\frac{\partial u}{\partial \vec{n}}\right|_{\partial\Omega} = 0 \ \text{and} \ u(x,0) = \widetilde{u}(x, \Delta t).$$

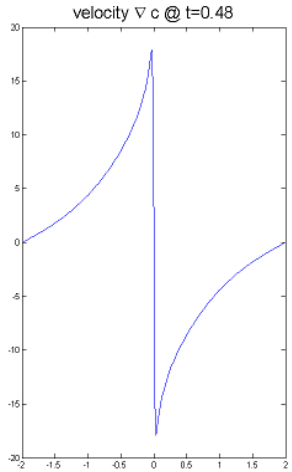
- Approximate the first equation by MUSCL scheme and approximate the second one by difference scheme discussed before.

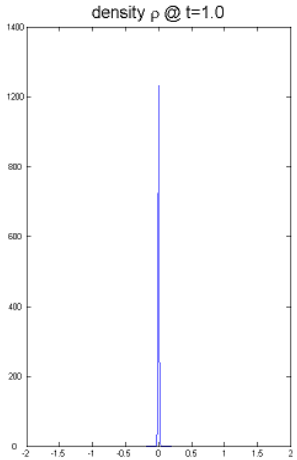
NUMERICAL OBSERVATION FOR K-S EQUATION IN 1-D

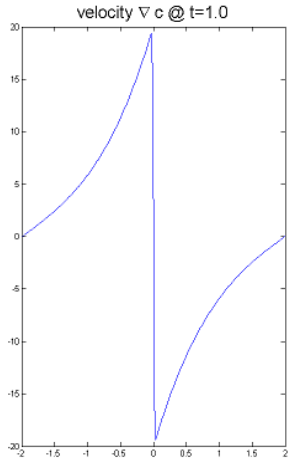












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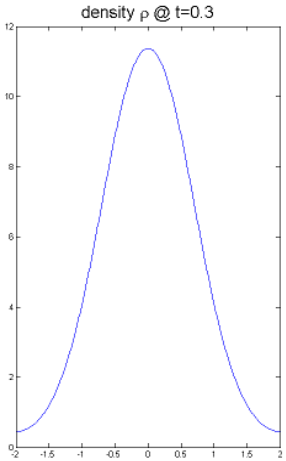
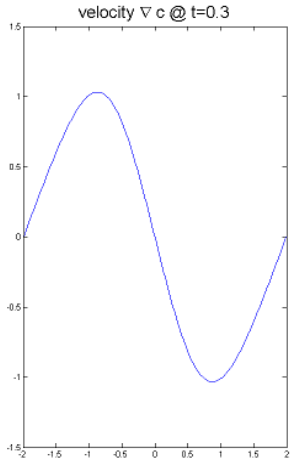
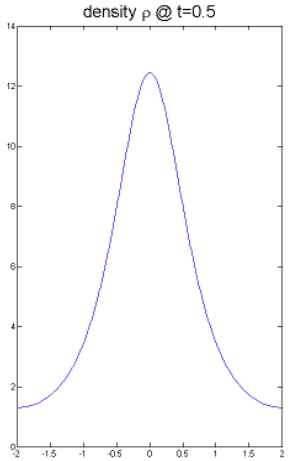
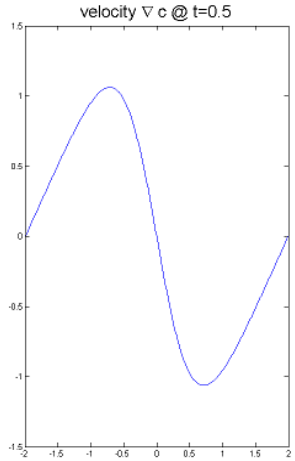
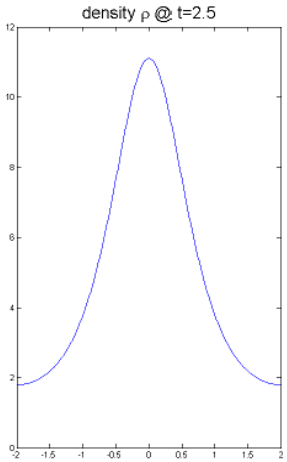
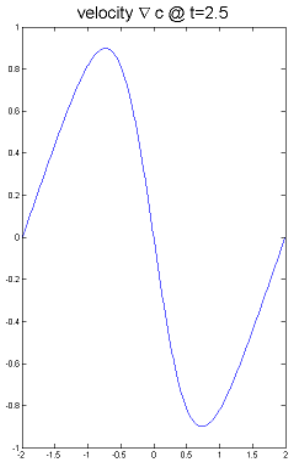




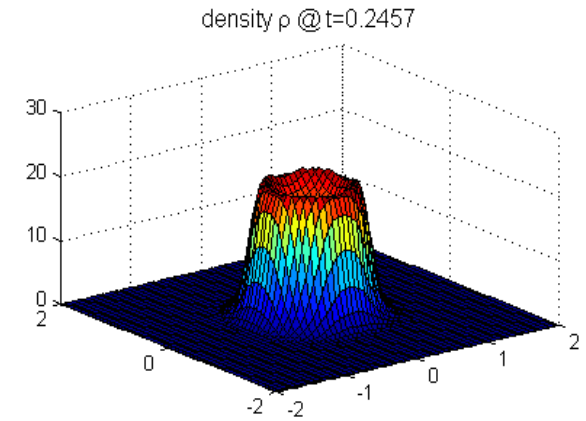


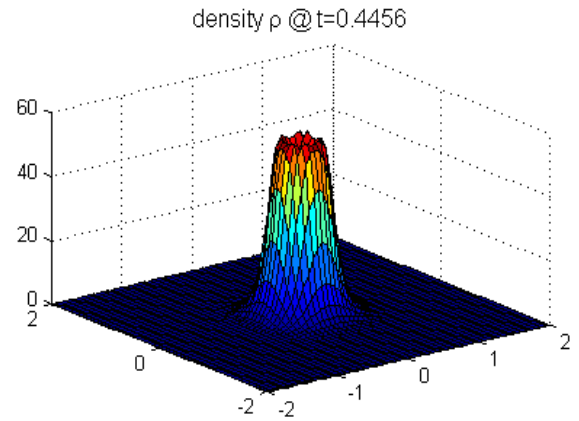


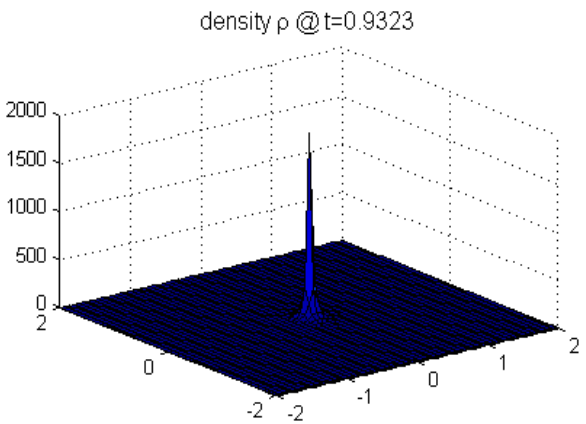


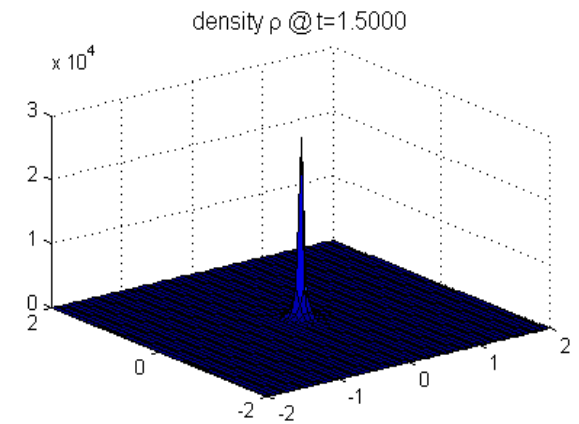


NUMERICAL OBSERVATION FOR K-S EQUATION IN 2-D









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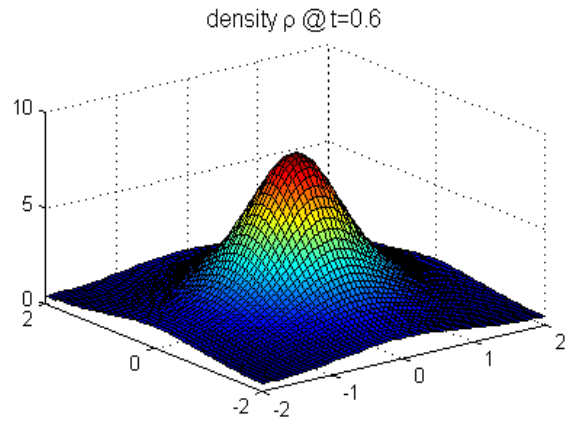
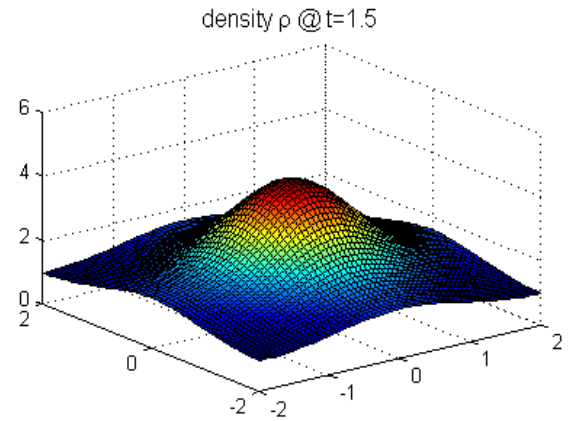
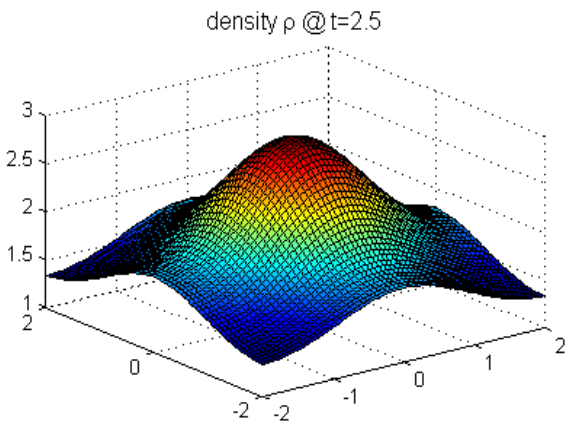
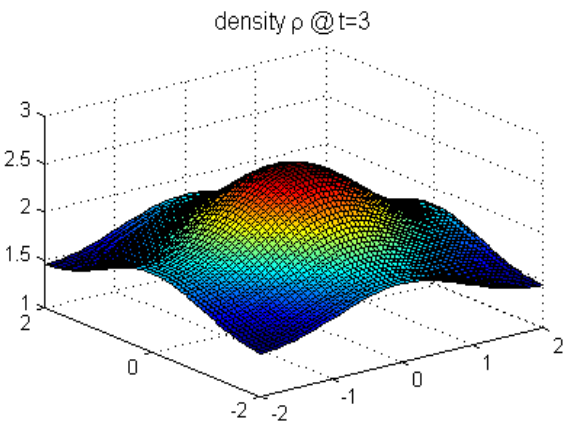
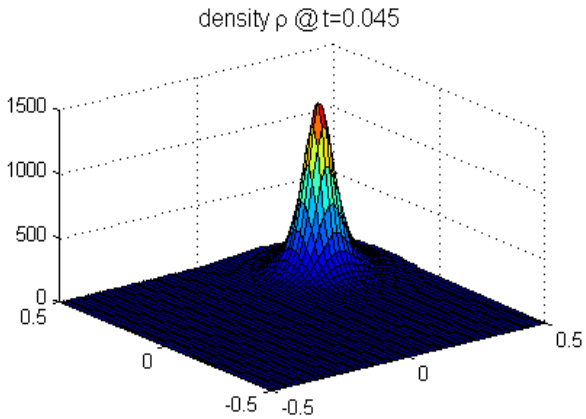


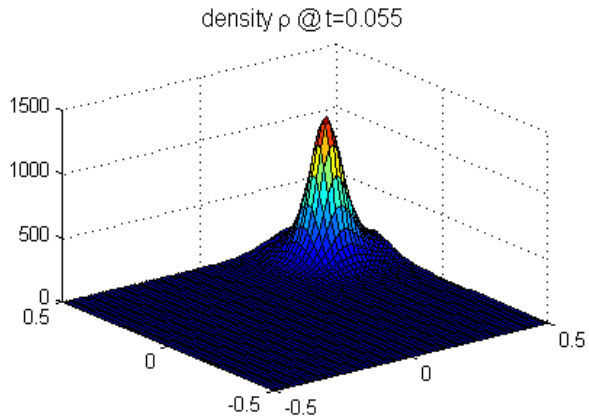


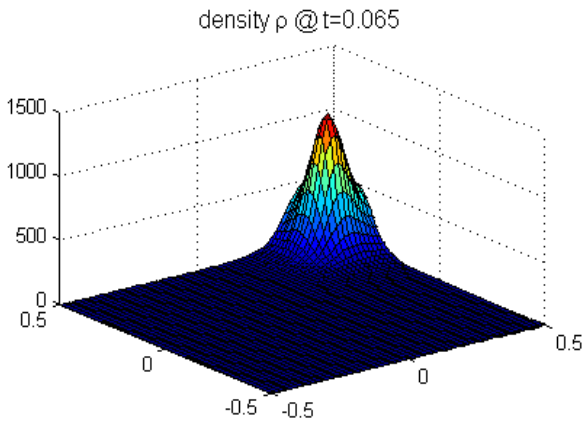


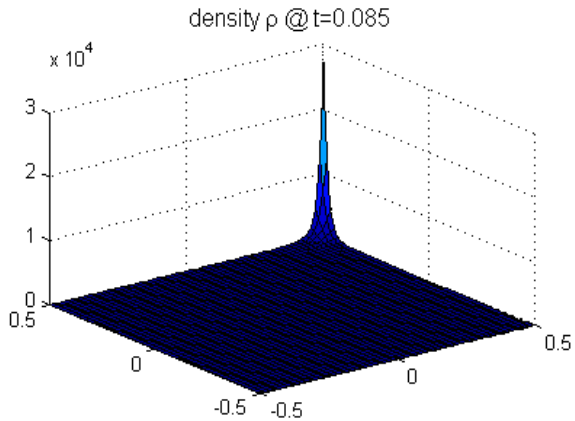


NUMERICAL OBSERVATION FOR K-S EQUATION IN 2-D









ESTIMATE DIFFUSION AND CHEMOTAXIS RATE

- Analogue to nonlinear regression, but way more complicated as the mean function is solution of a system of PDE's
- Early work includes Fister and McCarthy (2007), Yasmin (2009) etc.
- For constant diffusion and chemotaxis rates, the formulation is similar to least squared methods with penalty terms

$$(\chi^*, \mu^*) = \text{argmin}_{\mathbb{R}^{2+}} ||Z_i - F(\chi, \mu)||_{L^2(\Omega \times [0,T])} + G_\lambda(\chi, \mu)$$

F is an implicit function representing solution of PDE and G_λ is a penalty function (recall that LSE for linear model with penalties $\beta^* = \text{argmin}_{\mathbb{R}^p} \sum_{i=1}^{N} (Y_i - X\beta)^2 + g_\lambda(\beta)$).

A MORE GENERAL FORMULATION

- A general form (Liu, Sacks, Su and Zhou 2009): considering chemotaxis model

$$\begin{cases} u_t + \text{div}(\chi(c, |\nabla c|)\nabla c \cdot u) = \text{div}(\mu(c, |\nabla c|)\nabla u) \\ c_t - \text{div}(D(c, |\nabla c|)\nabla c) = \beta u - \alpha c. \end{cases} \tag{7}$$

and given data $z^{\delta}_{i,x} = (u(t_i, x) + \delta, c(t_i, x) + \delta)$ with $\delta \sim N(0, \varepsilon)$

$$(\chi^*, \mu^*, D^*) = \text{argmin} \frac{M}{2} \sum_{i,x} ||z^{\delta}_{i,x} - F(P)_{i,x}||^2 + G_{\alpha}(P)$$

F is the inverse operator associate to the PDE system, P is the projection of χ, μ, D on phase space, and G is Tikhonov regularization operator

SOME KNOWN RESULTS AND CHALLENGES

- The parameters for inverse problem of chemotaxis process are estimable (exists);
- The global identifiability issue remains open (given data, the parameters may not be uniquely determined);
- The resulting optimization problem is very challenging (the gradient and Hessian formulation are quite involved);
- The uncertainty from data is not modeled appropriately and inference on estimated parameters is hard to drawn;
- Bayesian methods might be helpful in this context (Steward 2009, 2010, 2012; Morris 2006; use Bayesian method to attack parameter estimation on PDE parameters).

SUMMARY

- Chemotaxis process is modeled by PDE system
  - Reaction-convection-diffusion equations is used to model chemotaxis process of population
  - Reaction-diffusion system is used to model the chemical diffusion
- PDE models: when to use it? why to use it? how to setup it?
- Theoretical study: existence, uniqueness, initial condition dependence.
- Theoretical exploration: stability of solution to perturbation of parameter, boundary conditions, stability with respect to time, special geometry of solution
- Numerical simulation: finite difference, finite volume and finite element
- Parameter estimation: starting from sum of square, Tikhonov regularization, and Bayesian?

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- Any questions?