(almost) All Life occurs in a Plasma of Spherical Ions in water

Na^+, K^+ , Ca^{++} , and Cl^-

each with a different diameter

Ion Diameters *Pauling Diameters*	
Ca^{++}	1.98 Å
Na^+	2.00 Å
K^+	2.66 Å

Ions are involved in most of biology

Ions are controlled by ion channels that are natural nano-valves*

<u>Ions</u> control all electrical activity in cells

<u>Ions</u> produce signals of the nervous system

<u>Ions</u> coordinate contraction in skeletal muscle

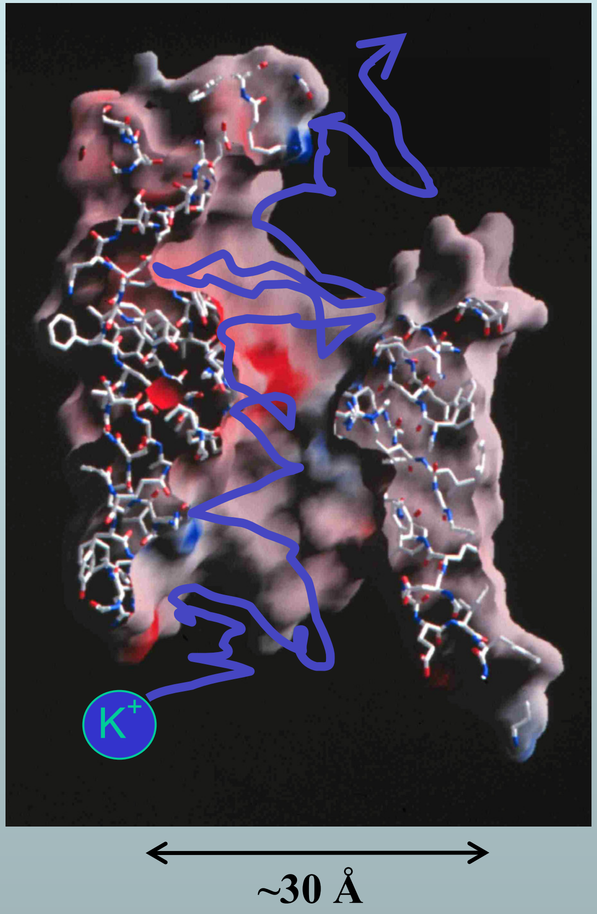
<u>Ions</u> coordinate contraction in the heart, allowing the heart to function as a pump

<u>Ions</u> are involved in secretion and absorption in all cells: kidney, intestine, liver, adrenal glands, etc.

<u>Ion channels</u> are involved in thousands of diseases and many drugs act on channels

<u>Ion channels</u> are proteins whose genes (blueprints) can be manipulated by molecular genetics

<u>Ion channels</u> have structures shown by x-ray crystallography in favorable cases.



*nearly <u>pico</u>-valves: diameter is 400 - 900 pico-meters

Charged Particles
in a Dielectric with Friction is
THE
Fundamental Problem in Plasmas,
including
Plasmas of Life

I am not qualified to discuss the importance of this problem in physical plasmas but to an outsider, it seems fundamental.

Seeking a Simple Description of the Brownian Motion of Charged Particles

Einstein's Brownian Particles are Uncharged

(nearly)

Everything Dissolved in Water is Charged

(somewhere)

<u>Conjecture</u>

Fluctuations in charge density are a significant –even dominant– source of Fluctuations in Plasmas

but

Einstein's treatment of Brownian motion does not discuss charge

Simplified Descriptions are Clearly Possible:

Ohm's Law works well for a wide range of ionic solutions

(Ohm's law involves ONLY charge)

Fick's law works well for a wide range of non-ionic solutions

(Fick's law involves only mass)

Self-consistent Simulation

Consider a random process in which charged particles move in an electric field created by their own charge and charge applied by boundary conditions. (No other applied fields are allowed)

1) Start with an overall neutral system
2) Choose a small volume
3) Count the number of particles of each type in that volume
4) Compute the electric field from the location and amount of charges
5) Allow the particles to move a small amount
6) Count again, etc.

Construct graphs of number density (‘concentration’) of particles vs. time and location.

Typical Time Series

$[X]$ = number of X **Time =**	**1**	**2**	**3**	**...**
Number of Na^+ $[Na^+]$	7	6	$[Na^+]$	...
Number of K^+ $[K^+]$	3	2	$[K^+]$	...
Number of Cl^- $[Cl^-]$	9	9	$[Cl^-]$	...
Number of Positive Charges	10	8	$[Na^+]+[K^+]$	...
Number of Negative Charges	9	9	$[Cl^-]$	...
Net Charge *Q* *(units: number of charges)*	+1	-1	$[Na^+]+[K^+]-[Cl^-]$	...
Number of Particles *N*	19	17	$[Na^+]+[K^+]+[Cl^-]$	...

Typical Time Series

	Time =	**1**	**2**	**3**	**...**
1) Number of Na^+	$[Na^+]$	0	6	$[Na^+]$	...
2) Number of K^+	$[K^+]$	**3**	**2**	$[K^+]$	...
3) Number of Cl^-	$[Cl^-]$	9	9	$[Cl^-]$	...

1) Gives equation for $[K^+]$

2) Gives equation for [Na+]

3) Gives equation for $[Cl^-]$

Variables [Na^+], [K^+], [Cl^-]

are **highly correlated**

so we have severe ‘closure’ problems

Time Series of

Time =	**1**	**2**	**3**	**...**
1) Net Charge *Q* *(units: number of charges)*	+1	-1	$[Na^+]+[K^+]-[Cl^-]$	...
2) Number of Particles *N*	19	17	$[Na^+]+[K^+]+[Cl^-]$	...

1) Gives equation for ***Q***

2) Gives equation for ***N***

Variables

$$Q = [Na^+]+[K^+]-[Cl^-]$$

$$N = [Na^+]+[K^+]+[Cl^-]$$

are **almost uncorrelated**

(we know from experiments and common sense)

so (I imagine)

we have almost no closure problems

Challenge

We know PDE's for $[Na^+]$, $[K^+]$, $[Cl^-]$.

What are the PDE's for ***Q*, *N*,** and $[Cl^-]$?

Challenge

How do we "change variable"?

How do we construct the counting process for charge and density?

Charged Brownian Motion in Langevin Form

Frictional Force

White Noise

$$\ddot{x}(t)_j^+ + \gamma_j^+ \dot{x}(t)_j^+ = \frac{\boldsymbol{F}_j^+}{m_j^+} + \sqrt{\frac{2\gamma_j^+ k_B T}{m_j^+}}\ \dot{w}(t)_j^+ \qquad j = 1, 2, \ldots N$$

Electrical Force

Similar Equation for location $x(t)_k^-$ of negative species *k*

Electrical Force

$$\boldsymbol{F}_j^+$$

Electrical Force is computed

1) from solution of Poisson's equation,

or by applying

2) Coulomb's law to all other charges

What has been done?

We start with Langevin equations of charged particles

Simplest stochastic trajectories
are
Brownian Motion of Charged Particles

Gouy-Chapman, (nonlinear) Poisson-Boltzmann, Debye-Hückel,
are models with similar resolution
but constrained to equilibrium, i.e., zero flux of all species.
Devices do not exist at equilibrium

Once we learn to count Trajectories of Brownian Motion,
we can count trajectories of <u>Molecular Dynamics</u>

Equilibrium

Configurations

Boltzmann Distribution

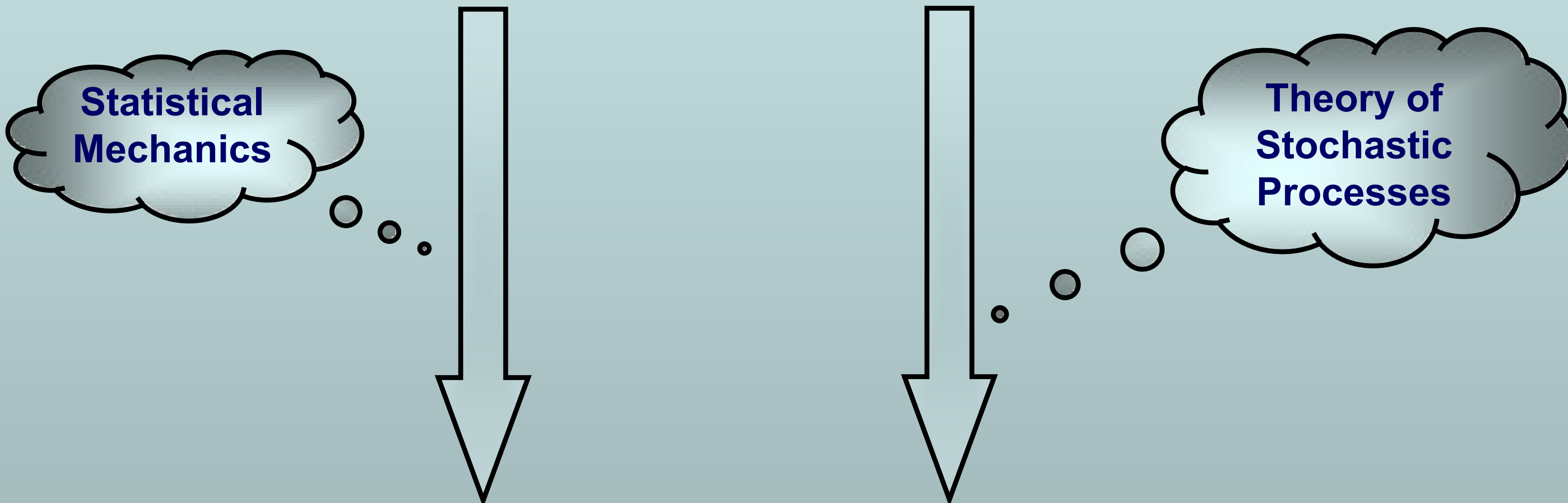
$$\lim N, V \to \infty$$

Nonequilibrium

Trajectories

Fokker Planck Equation

Finite OPEN System



Thermodynamics

Device Equation

Schuss, Nadler, and Eisenberg

Langevin Equations

Positive ***cat*ion**, e.g., p = Na^+

$$\ddot{x}_k^p - \frac{f_k^p(\tilde{x};q_k)}{m} = -\gamma\dot{x}_k^p + \sqrt{\frac{2\gamma kT}{m}}\dot{w}_k^p$$

Negative ***an*ion**, e.g., n = Cl^-

$$\underbrace{\ddot{x}_k^n - \frac{f_k^n(\tilde{x};q_k)}{m}}_{\text{Newton's Law}} = \underbrace{-\gamma\dot{x}_k^n + \sqrt{\frac{2\gamma kT}{m}}\dot{w}_k^n}_{\text{Friction \& Noise}}$$

Electric Force
from **all charges** including
Permanent charge of Protein,
Dielectric Boundary charges,
Boundary condition charge

Schuss, Nadler, Eisenberg

Electric Force from Poisson Equation

Electric Force
from **all charges** including
Permanent charge of **Protein**,
Dielectric Boundary charges,
Boundary condition charge

Excess
'Chemical'
Force

$$f_k^{p}(\vec{\mathbf{x}}) = f_{xs} + \overbrace{q_k(\vec{\mathbf{x}})\,\mathbf{div}\left(\varepsilon(\vec{\mathbf{x}})\vec{\mathbf{E}}\right)} = \frac{e}{\varepsilon_0}\mathrm{P}(\mathbf{x}) + \frac{e}{\varepsilon_0}\sum_i z_i\rho_i(\mathbf{x})$$

Implicit Solvent
'Primitive' Model
or
Primitive Solvent Model

Schuss, Nadler, Eisenberg

From Trajectories to Probabilities

Main Result: Theory of Stochastic Processes

Joint probability density of position and velocity

$$p\left(\tilde{x},\tilde{v}\right)=\mathbf{Pr}\left\{\left\{x_j,v_j\right\}_{j=1}^{2N}\right\}; \quad N = \text{Number of Particles}$$

satisfies a Fokker Planck equation

$$0=\sum_j \mathsf{L}_j^p\, p\left(\tilde{x},\tilde{v}\right)+\sum_j \mathsf{L}_j^n\, p\left(\tilde{x},\tilde{v}\right)$$

with Fokker Planck Operator

$$\mathsf{L}_j^c p = -v_j^c \cdot \nabla_{x_j^c}\, p + \nabla v_j^c \cdot \left(\gamma v_j^c - \frac{f_j^c}{m_j^c}\right) p + \nabla \cdot \nabla_{v_j^c}\, \frac{\gamma k T}{m_j^c}\, p$$

Coordinates are positions and velocities of N particles in 12N dimensional phase space

Schuss, Nadler, and Eisenberg

Conditional PNP

Electric Force $\nabla\bar{\phi}$ depends on Conditional Density of Charge

$$\nabla_y \cdot \left[\frac{\varepsilon_0\varepsilon(y)}{e}\nabla_y \bar{\phi}(y\,|\,x)\right] = P(y) + \rho_+(y\,|\,x) - \rho_-(y\,|\,x)$$

Channel Protein

Closures or **Approximations** Needed

Nernst-Planck gives UNconditional Density of Charge

$$\nabla_x \cdot \left[\frac{1}{m\gamma(x)}\rho_+(x)\left[e\nabla_y \bar{\phi}(y\,|\,x)\Big|_{y=x} - DBF\right]\right] = 0$$

Mass

Friction

Schuss, Nadler, Eisenberg

Closure by Hand

Counting at low resolution gives

'Semiconductor Equations'

Poisson-Nernst-Planck (PNP)

Only contains correlations of means

Gouy-Chapman, (nonlinear) Poisson-Boltzmann,
Debye-Hückel,
are siblings with similar resolution

but without current or flux of any species

Devices do not exist at equilibrium

PNP in 3D

Poisson's Equation

$$-\varepsilon_0 \nabla \cdot \left(\varepsilon(\mathbf{x}) \nabla \phi(\mathbf{x}) \right) = e\mathrm{P}(\mathbf{x}) + e\sum_i z_i \rho_i(\mathbf{x})$$

Channel Protein

Drift-diffusion & Continuity Equation

$$\nabla \cdot \mathbf{J}(\mathbf{x}) = 0; \quad -\mathbf{J}_i(\mathbf{x}) = D_i(\mathbf{x}) \rho_i(\mathbf{x}) \frac{1}{kT} \nabla \mu_i(\mathbf{x})$$

Chemical Potential

Closure by Hand!

$$\mu_i(\mathbf{x}) = z_i e\phi(\mathbf{x}) + kT \ln\left(\frac{\rho_i(\mathbf{x})}{\rho^*} \right) + \mu_i^{\mathrm{ex}}(\mathbf{x})$$

Special Chemistry

Solving semiconductor equations requires a trick

Poisson Equation

and

Nernst Planck Equation

(Fick's Law for charged particles)

are solved together

by

Gummel iteration

Poisson → Transport → Poisson → Transport

Or much better

(but much harder)

Newton Iteration

Electrodiffusion of charged, hard spheres

Correlations put in by Hand

Closure by Hand

How well can we do biology with correlations done by hand?

Questions?