Multi-scale Modeling of Electric Activity of Spiny Dendrites in the Hippocampus

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joint work with

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in collaboration with

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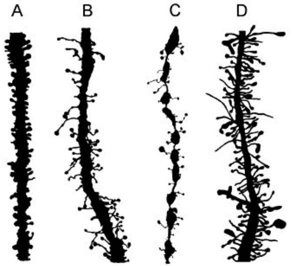
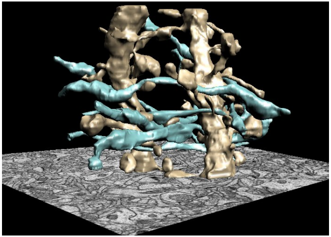
Outline

Outline

Motivation: Neuronal Modeling



Fiala, Spacek, and Harris 2002

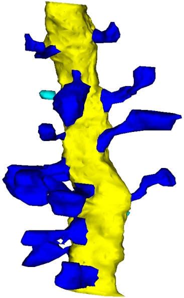


- Dendritic spine distribution and shape in the hippocampus correlates with certain types of brain disease.
  - A) Neurologically normal (6 months).
  - B) Mentally retarded (12 months).
  - C) Alzheimer's (adult).
  - D) Fragile X syndrome (adult).

- Simulating the effect of spine modification requires accurate geometry and stable methods for modeling electric activity.

Problem Statement

The PDE governing electric activity depends on the scale considered:



- Micron scale (10^{-6} m):
  Electrodynamic Equation

$$\frac{d}{4R_i}\frac{\partial^2 V}{\partial z^2} = C_m \frac{\partial V}{\partial t} + \frac{V - V_0}{R_m}$$

- Nanometer scale (10^{-9} m):
  Electrodiffusion Equations

$$\begin{cases} \vec{J}_k &= -\left(\nabla c_k + \frac{F z_k}{RT} c_k \vec{E}\right) \\ 0 &= \text{div}\left(\epsilon \vec{E}\right) + \sum c_k z_k F \\ \vec{E} &= \nabla \phi \\ 0 &= \frac{\partial}{\partial t} c_k + D_k \text{div}\, \vec{J}_k \end{cases}$$

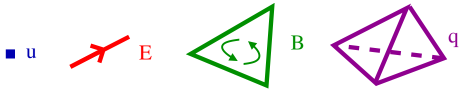
Problem Statement

Characterize the geometry-sensitive coupling parameters between these equations and cast both into a consistent discrete exterior calculus framework.

Outline

Why consider differential forms for models?

- Differential *k*-forms model *k*-dimensional physical phenomena.



- The exterior derivative *d* generalizes common differential operators.

$$\Lambda^0(\Omega) \xrightarrow[\text{grad}]{d_0} \Lambda^1(\Omega) \xrightarrow[\text{curl}]{d_1} \Lambda^2(\Omega) \xrightarrow[\text{div}]{d_2} \Lambda^3(\Omega)$$

- The Hodge Star transfers information between complementary dimensions.

$$\Lambda^0(\Omega) \longleftarrow * \longrightarrow \Lambda^3(\Omega)$$

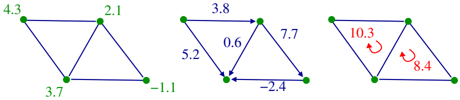
$$\Lambda^1(\Omega) \longleftarrow * \longrightarrow \Lambda^2(\Omega)$$

Fundamental Theorem of Discrete Exterior Calculus

Stable computational methods must recreate the essential properties of smooth exterior calculus on the discrete level.

What are discrete differential forms?

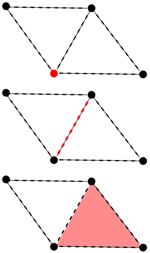
- Discrete differential *k*-forms are *k*-cochains, i.e. linear functions on *k*-simplicies.



- The discrete exterior derivative is $\mathbb{D} = (\partial)^T$, the transpose of the boundary operator.

$$\mathcal{C}^0 \xrightarrow[\text{(grad)}]{\mathbb{D}_0} \mathcal{C}^1 \xrightarrow[\text{(curl)}]{\mathbb{D}_1} \mathcal{C}^2 \xrightarrow[\text{(div)}]{\mathbb{D}_2} \mathcal{C}^3$$

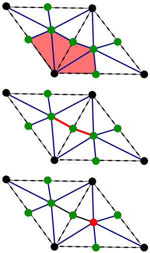
- The discrete Hodge Star transfers information between complementary dimensions on dual meshes.



$$\Lambda^0(\Omega) \longleftarrow \mathbb{S} \longrightarrow \Lambda^2(\Omega)$$

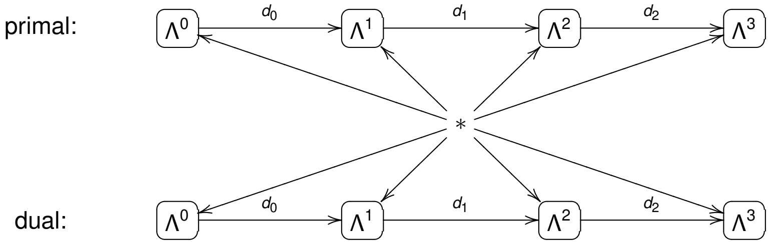
$$\Lambda^1(\Omega) \longleftarrow \mathbb{S} \longrightarrow \Lambda^1(\Omega)$$

$$\Lambda^2(\Omega) \longleftarrow \mathbb{S} \longrightarrow \Lambda^0(\Omega)$$

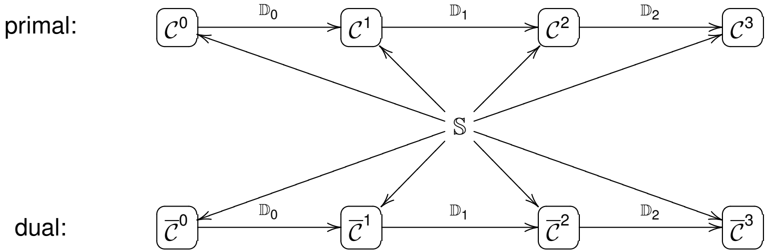


An overview of DEC theory

Smooth exterior calculus:



Discrete exterior calculus:



Selected Prior Work

- Importance of differential geometry in computational methods for EM:

BOSSAVIT *Computational Electromagnetism* Academic Press Inc. 1998

- Adoption of DEC techniques by national laboratory scientists:

CASTILLO, KOINING, RIEBEN, STOWELL AND WHITE *A novel methodology for robust computational electromagnetics* Technical report, LLNL, 2003

- Primer on DEC theory and program of work:

DESBRUN, HIRANI, LEOK AND MARSDEN *Discrete Exterior Calculus* arXiv:math/0508341v2 [math.DG], 2005

- Applications of DEC to general relativity, Darcy flow, and elasticity problems:

FRAUENDIENER *Discrete diffrential forms in general relativity* Classical and Quantum Gravity, 23(16):S369–S385, 2006

HIRANI, NAKSHATRALA AND CHAUDHRY *Numerical method for Darcy Flow derived using Discrete Exterior Calculus* arXiv:0810.3434v1 [math.NA], 2008

YAVARI *On geometric discretization of elasticity* Journal of Mathematical Physics, 49(2):022901-1–36, 2008

Outline

Electrodiffusion Equations

c_k	concentration of kth ion species
$\vec{J}_k$	flux of kth ion species
$\vec{E}$	electric field
ϕ	electric potential

D_k	diffusion coefficient
F	Faraday constant
R	gas constant
T	temperature
z_k	ion valence
ϵ	dielectric coefficient

- Nernst-Planck Equation:

$$\underbrace{-\vec{J}_k}_{\text{total ion flux}} = \underbrace{\nabla c_k}_{\substack{\text{flux due to diffusion} \\ \text{(Fick's law)}}} + \underbrace{\frac{Fz_k}{RT} c_k \vec{E}}_{\substack{\text{flux due to drift in electric field} \\ \text{(Ohm's law)}}}$$

- Poission's equation for electric potential:

$$\text{div}\left(\epsilon \vec{E}\right) = -\sum c_k z_k F, \quad \vec{E} = \nabla \phi$$

- Continuity Equation:

$$\underbrace{\frac{\partial}{\partial t} c_k}_{\text{time derivative of concentration}} = \underbrace{-D_k \text{div} \vec{J}_k}_{\text{change in total ion flux}}$$

Electrodiffusion Equations - Rewritten

$$\begin{cases} \vec{J}_k &= -\left(\nabla c_k + \frac{Fz_k}{RT} c_k \vec{E}\right) \\ 0 &= \text{div}\left(\epsilon \vec{E}\right) + \sum c_k z_k F \\ \vec{E} &= \nabla \phi \\ 0 &= \frac{\partial}{\partial t} c_k + D_k \text{div}\ \vec{J}_k \end{cases}$$

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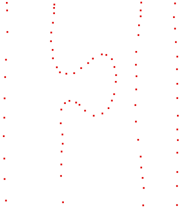
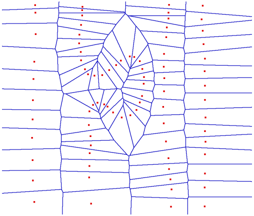
Where are the variables valued?

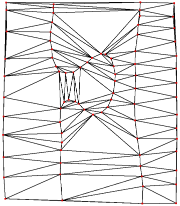
Surface points



Voronoi (primal) cells

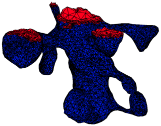


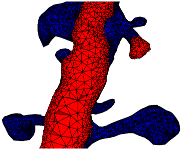
Delaunay (dual) cells

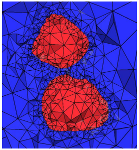


c_k	ion concentration	Delaunay tetrahedra
$\vec{J}_k$	ion flux	Delaunay faces
$\vec{E}$	electric field	Voronoi edges
ϕ	electric potential	Voronoi points

$$\begin{cases} \vec{J}_k &= -\left(\nabla c_k + \frac{Fz_k}{RT} c_k \vec{E}\right) \\ 0 &= \mathrm{div}\left(\epsilon \vec{E}\right) + \sum c_k z_k F \\ \vec{E} &= \nabla \phi \\ 0 &= \frac{\partial}{\partial t} c_k + D_k \mathrm{div}\, \vec{J}_k \end{cases}$$







Electrodiffusion Variables as k-forms

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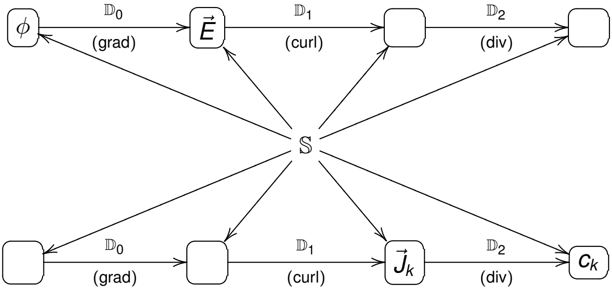
\end{cases}
$$

c_k	ion concentration	dual tetrahedra
$\vec{J}_k$	ion flux	dual faces
$\vec{E}$	electric field	primal edges
ϕ	electric potential	primal points

Primal (Voronoi)

Dual (Delaunay)



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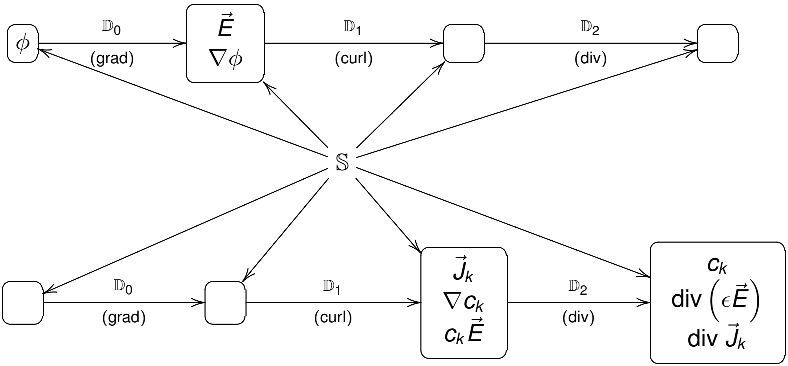

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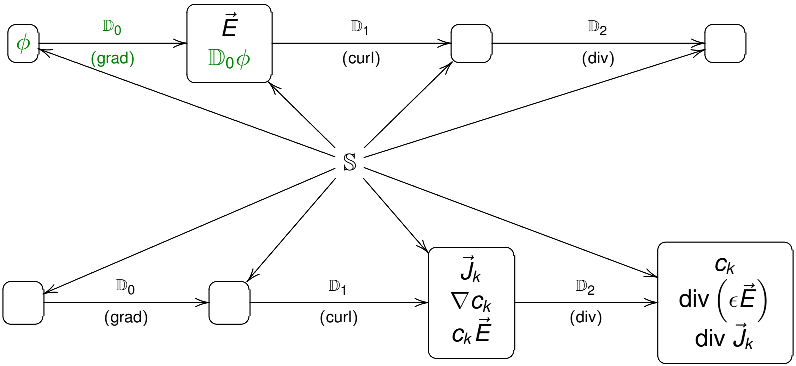

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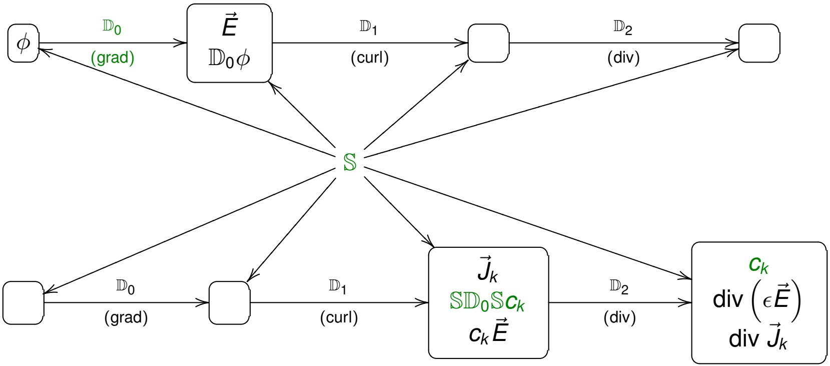

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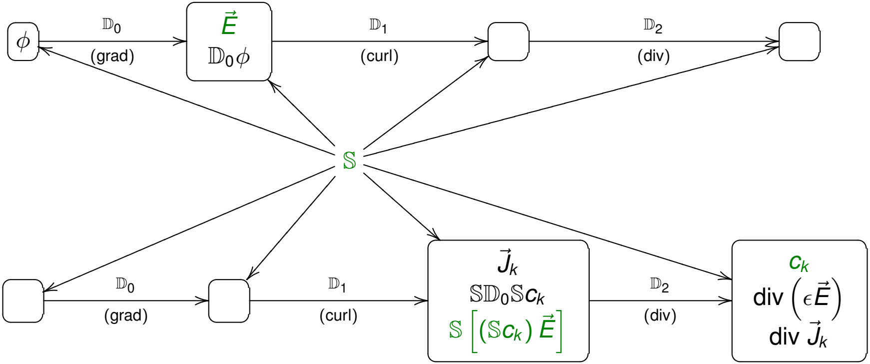

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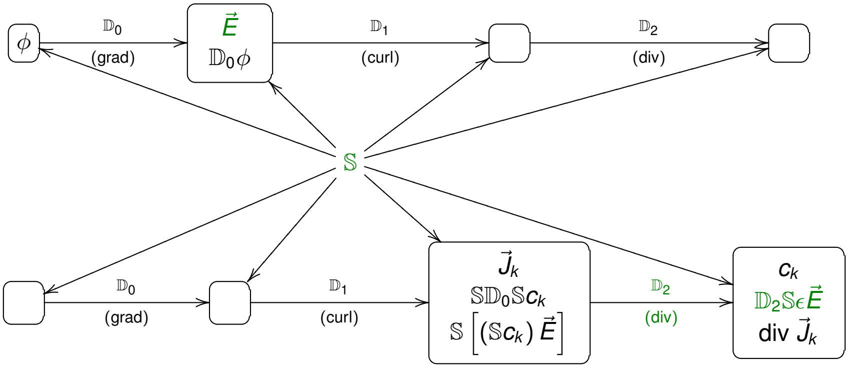

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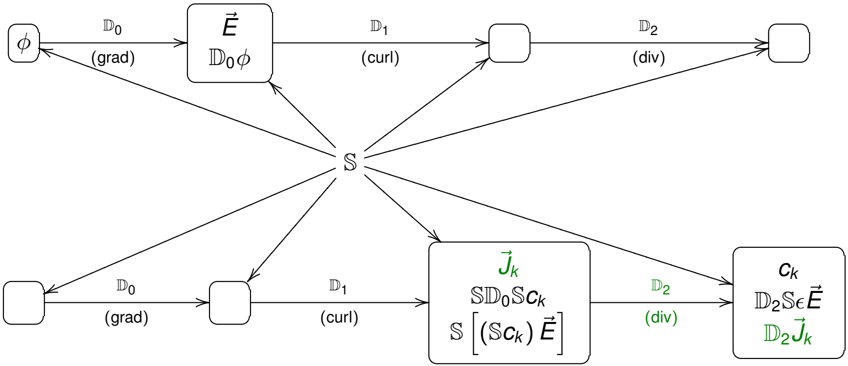


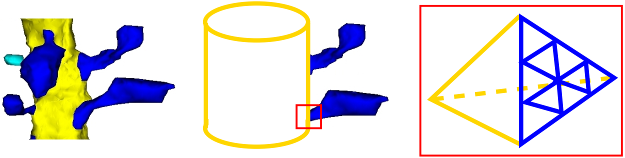
Outline

Coupling the Equations

$$\frac{d}{4R_i}\frac{\partial^2 V}{\partial z^2} = C_m \frac{\partial V}{\partial t} + \frac{V - V_0}{R_m}$$

V	voltage
z	axial direction
R_i	axial resistance
R_m	membrane resistance
C_m	membrane capacitance
V_0	resting potential

- Compartment model: $C_m \frac{dV}{dt} = -i_m + i_{ext}$
  - i_m = sum of trans-membrane currents
  - i_{ext} = sum of currents injected to intracellular space



V in compartment $= \phi$ at Voronoi points of interface

$$(\text{summand in } i_{ext}) \cdot \left(\frac{\text{interface surface area}}{\text{compartment surface area}}\right) = \vec{J}_k \text{ at Delaunay faces of interface}$$

Next Steps

- Define suitable interpolants for each of the electrodiffusion variables based on the Discrete Exterior Calculus analysis.
- Prove stability of the associated numerical method.
- Consider subtleties arising from boundary conditions (stay tuned for Dr. Rand's talk. . .)

Questions?

- Slides available at http://www.ma.utexas.edu/users/agillette/
- Thanks to the organizers for the invitation!