

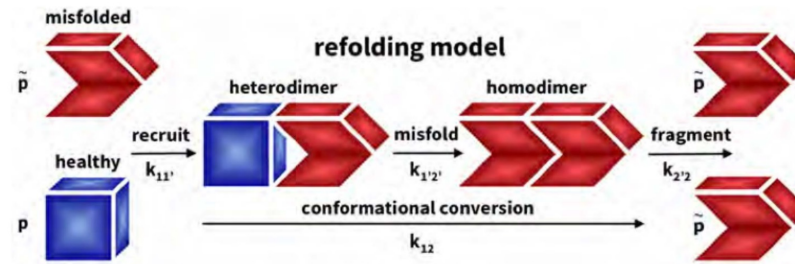
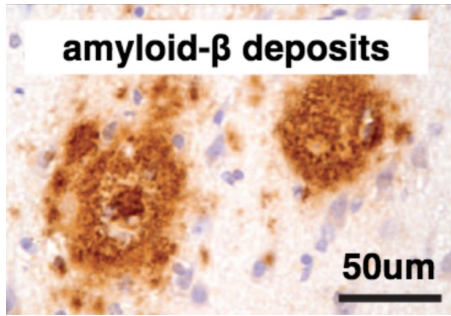
POSTER SESSION BLITZ  
TUESDAY JUNE 13, 2023

Andrew Ahern, University of Oxford  
Azzam Alfarraj, Michigan State University  
Jiahui Chen, Michigan State University  
Chidozie Chukwu, Wake Forest University  
Ruby Kim, University of Michigan  
Chunyan Li, University of South Carolina  
Tin Phan, Los Alamos National Laboratory  
Yuchi Qiu, Michigan State University  
Dexuan Xie, University of Wisconsin-Milwaukee

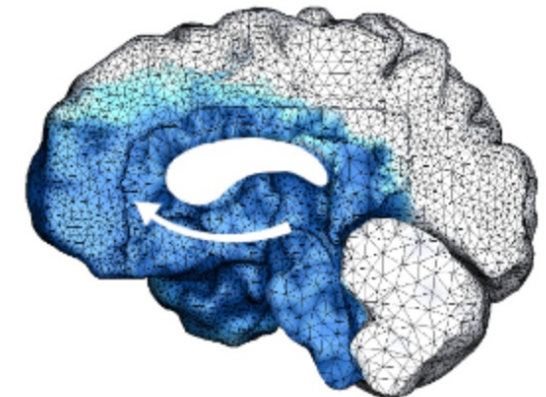
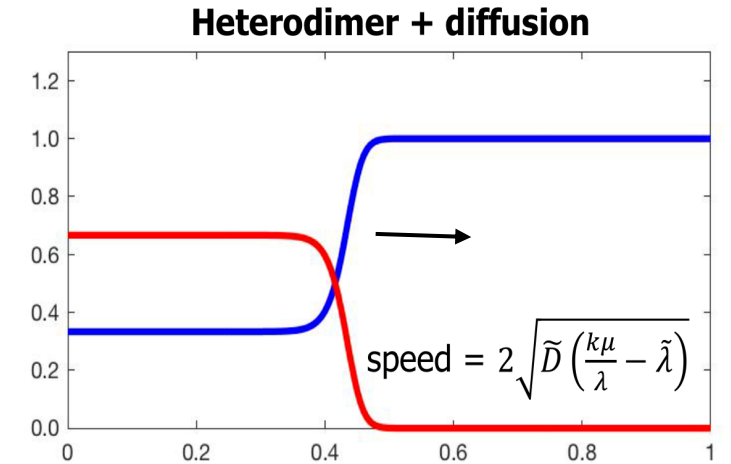
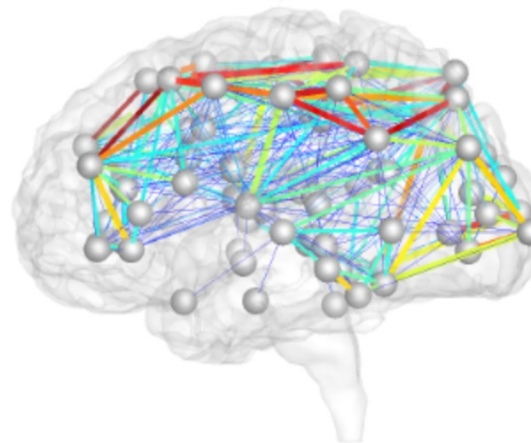
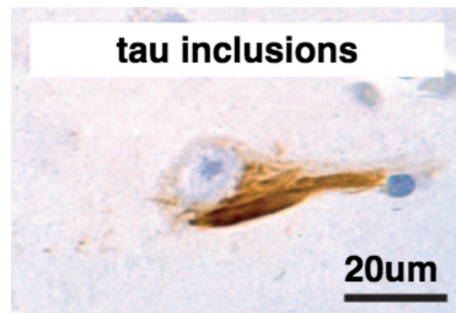
# Amyloid-capillary dynamics in Alzheimer's

Andrew Ahern (Oxford)

## Review of general methodology



Local dynamics + Brain architecture

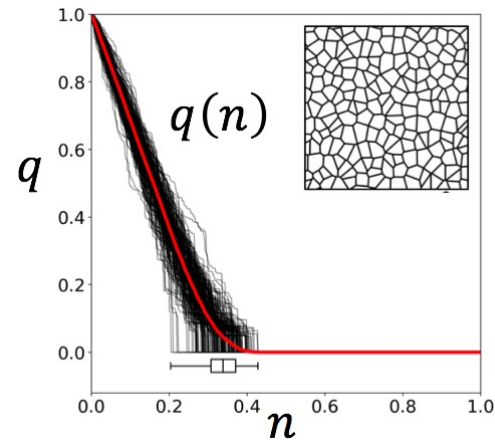
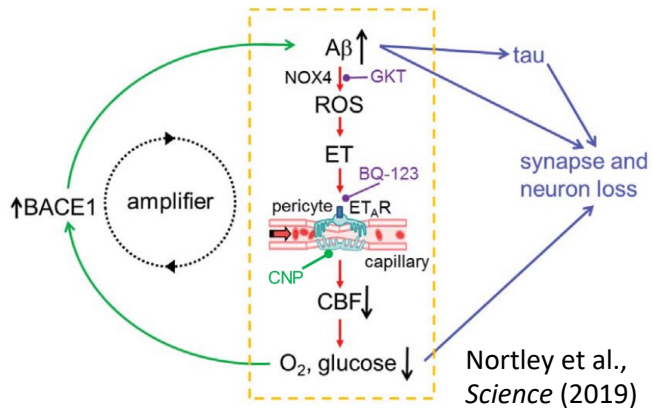


Weikenmeier et al.,  
*Phys Rev Lett* (2018)

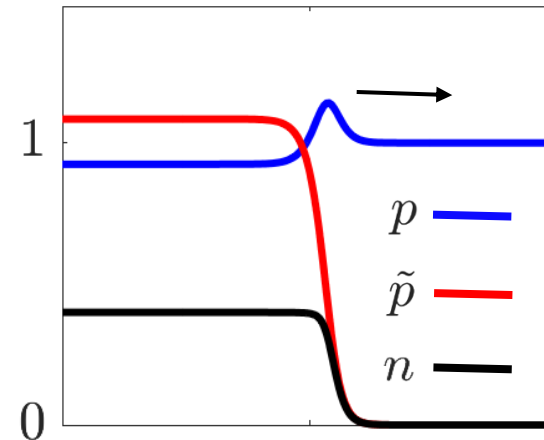
# Amyloid-capillary dynamics in Alzheimer's

## Andrew Ahern (Oxford)

### Amyloid & capillaries

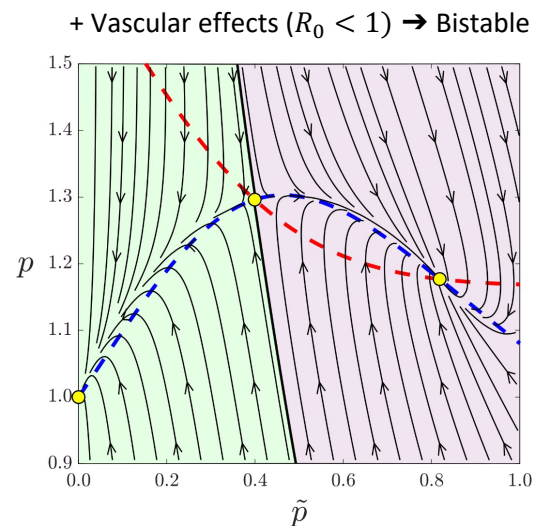
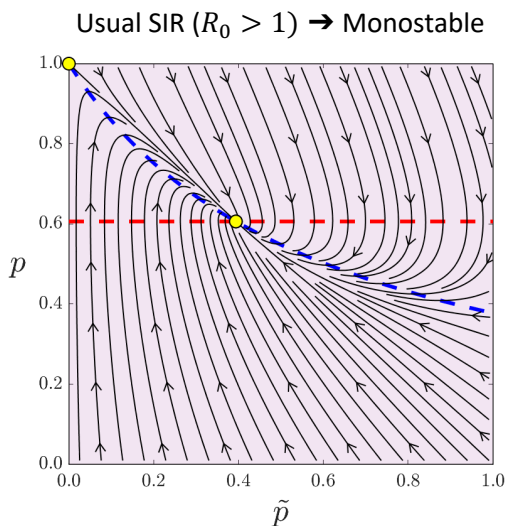


### Spatial dynamics

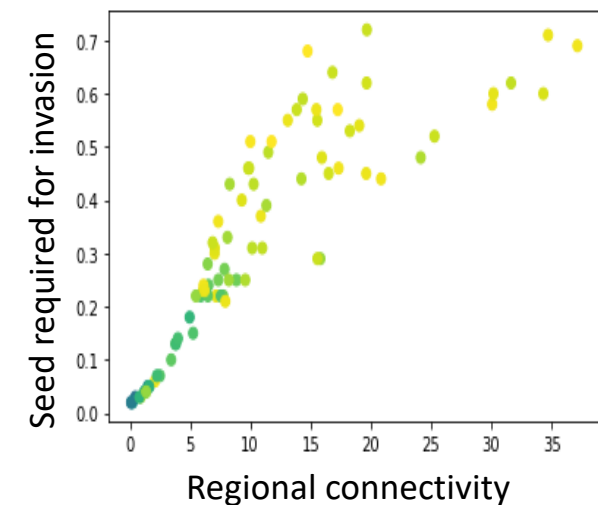
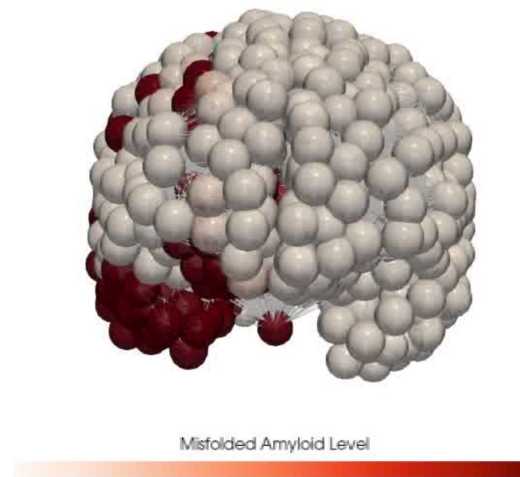


- Pushed fronts of invasion/retreat
- Meta-stability, excitability
- Propagation failure

### Local dynamics



### Network spatial dynamics



# GEOMETRIC ALGEBRA APPROACHES TO PROTEIN-PROTEIN DOCKING

AZZAM ALFARRAJ, GUO-WEI WEI

## What is protein-protein docking?

- Predicting the **preferred orientation** of interactive proteins, when they are bound to form a stable complex.

## Computational methods

- Sampling **billions** of putative complex structures.
- **Computationally expensive**, using rotations and translations extensively.

## Why geometric algebra?

- Efficient acceleration is achieved in either the **rotational** or the translational subspace.
- Geometric algebra **overpasses** in performing operations in a far more compact and efficient way, especially **rotations** here.

## Maxwell's Equations in GA:

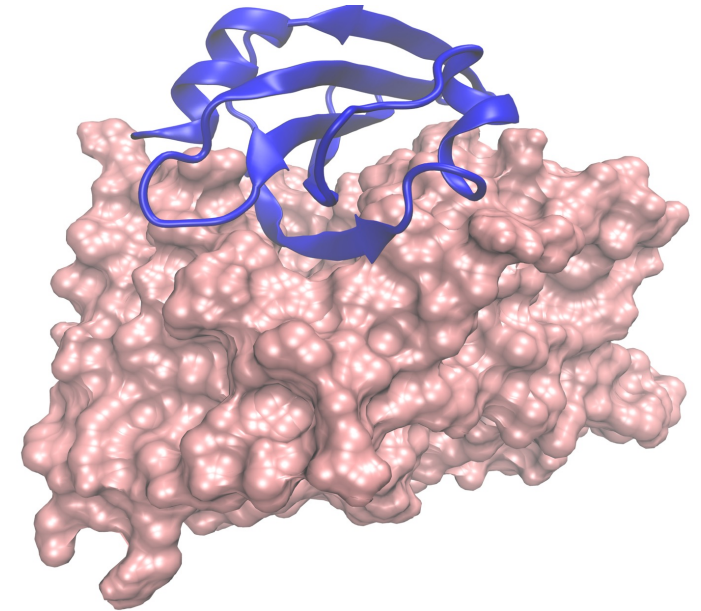
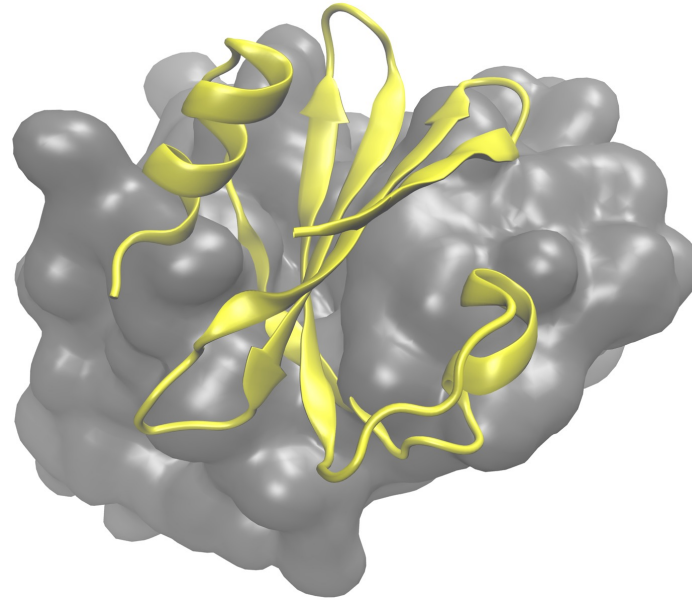
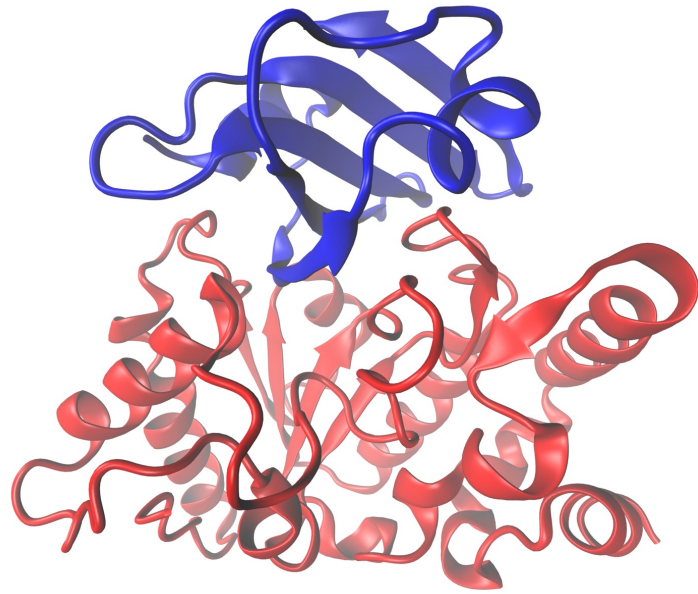
$$\left. \begin{aligned} \nabla \times H &= J + \partial D / \partial t \\ \nabla \times E &= -\partial B / \partial t \\ \nabla \cdot D &= \rho \\ \nabla \cdot B &= 0 \end{aligned} \right\} \equiv \nabla \mathcal{F} = \mathcal{J}$$

## Rotation in GA

$$b = RaR^{-1}$$

$$\begin{aligned} R &= R_\psi R_\theta R_\phi \\ &= e^{-e_{12}\phi/2} e^{-e_{23}\theta/2} e^{-e_{12}\psi/2} \end{aligned}$$

# RESULTS OF ENZYME-INHIBITOR TUDI:



Energy		
Model #	GA	FMFT
0	-880.01	-880.01
1	-876.91	-843.87
2	-843.87	-841.74
3	-841.74	-826.94

Cluster Size		
Model #	GA	FMFT
0	305	303
1	205	214
2	120	89
3	94	61

## Execution Time:

GA time: 5 min 42 sec

FMFT time: 6 min 31 sec



## **Evolutionary de Rham Hodge method**

Jiahui Chen Michigan State University

Artificial intelligence (AI) has emerged as a new paradigm for scientific discovery. However, AI modeling of biological data remains a challenge due to their intricate structural complexity, excessively high dimensionality, severe nonlinearity, and intrinsic multiscale. We devise differential geometry and algebraic topology to address these challenges. Specifically, we utilize persistent homology, a main workhorse in topological data analysis (TDA), to simplify biomolecular structure complexity and reduce their dimensionality. Since persistent homology is insensitive to homotopic shape evolution, we developed persistent Laplacians to capture non-topological shape changes in data by their non-harmonic spectra. For volumetric data, like molecular electron density of proteins, we proposed an evolutionary de Rham-Hodge method to extend the traditional Hodge Laplacian to a multiscale formulation. We introduced boundary-induced graph Laplacians to further reduced computational complexity. These new mathematical tools are paired with advanced machine learning algorithms, such as ensemble learning, manifold learning, graph neural networks, and transformers, to reveal the mechanisms of SARS-CoV-2 transmission and evolutions via infectivity strengthening and antibody resistance.

## Introduction

- Listeria is a Gram-positive facultatively anaerobic bacillus which was discovered by E.G.D. Murray in 1924, and in 1926, it was finally classified as *Listeria monocytogenes* [1]
- Ready-to-eat food (RTE) are foods that the producers intend for direct human consumption without further preparation. Some examples of RTE food products that have been linked to causing Listeriosis includes polony, vegetables, dairy products, smoked fish and cooked shellfish, unpasteurized milk, cheeses, sausages, hot dogs, deli meats.
- Cross-contamination is the process by which bacteria/microorganisms with harmful effects are unintentionally transferred from one substance or object to another, for example, during RTE production.
- Human Listeriosis is a zoonotic disease that results from consuming contaminated RTE food products.

## Motivation

Motivated by the work done in [2] and the recent outbreak of Listeriosis in South Africa in 2017/2018 with 1049 confirmed cases and been one of the world's most significant *Listeria* outbreaks. Nonetheless, sporadic Listeriosis outbreaks have also been recorded in other parts of the world including Canada, Europe, USA, and so on.

## Modeling

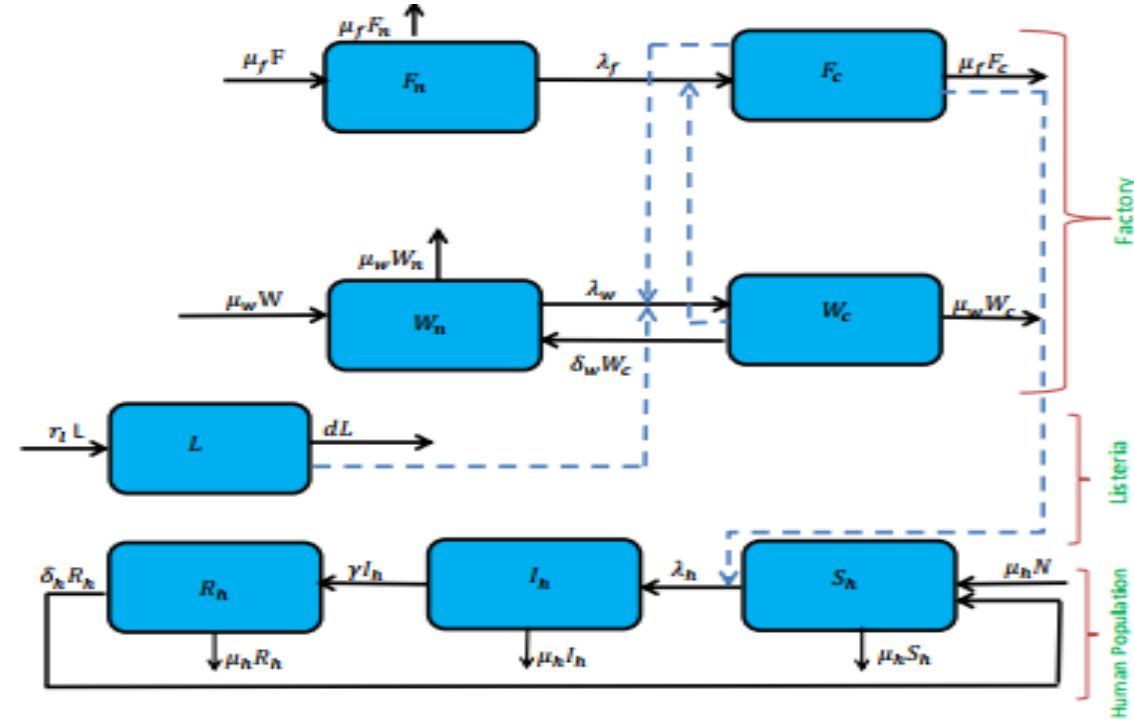


Fig. 1: Model flow diagram describing the Listeriosis dynamics and how it affects the human population.

The model exhibited three steady states: the disease-free equilibrium, Listeria-free, and endemic equilibrium points. Solving the steady states we found the Contamination Threshold

$$R_{wf} = \frac{\beta_3 \beta_4}{\mu_f (\mu_w + \delta_w)}$$

## Results

- The results show that reducing the number of contaminated workers and removing contaminated food products are essential in eliminating the disease in the human population.

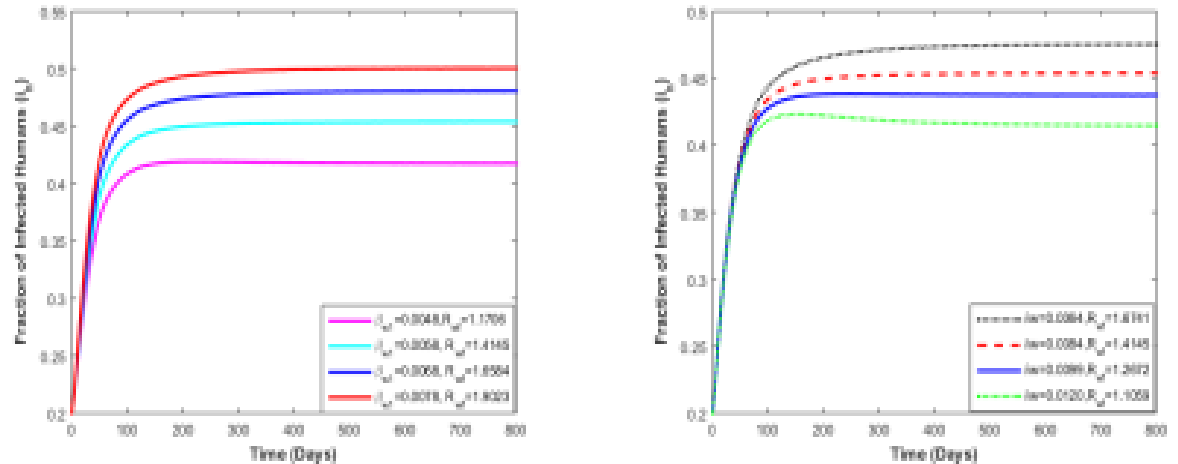


Fig. 3: Effect of  $\beta_w$  and  $\delta_w$  on the fractions of infected humans.

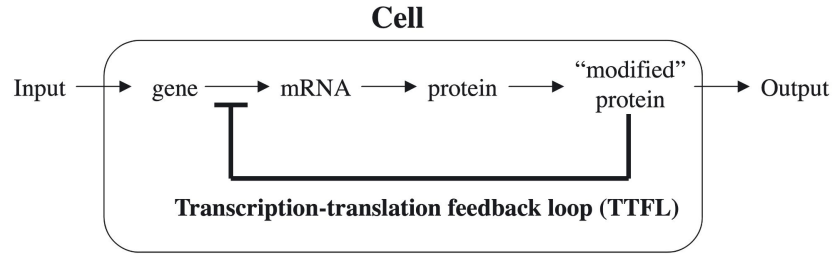
## References

- [1] Hof H., History and epidemiology of Listeriosis, FEMS Microbiol. Immunol., Blackwell Publishing Ltd Oxford, UK, Vol.35, no.3, pp.199--202, 2003.
- [2] Ivanek R., et al., Mathematical model of Listeria monocytogenes cross-contamination in a fish processing plant, Food Prot., Inter. Assoc. for Food Prot., Vol.67, no.12, pp.2688--2697, 2004.

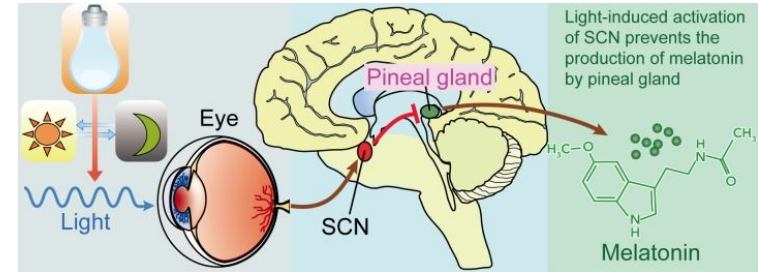


# The circadian clock, downstream physiology, and feedback

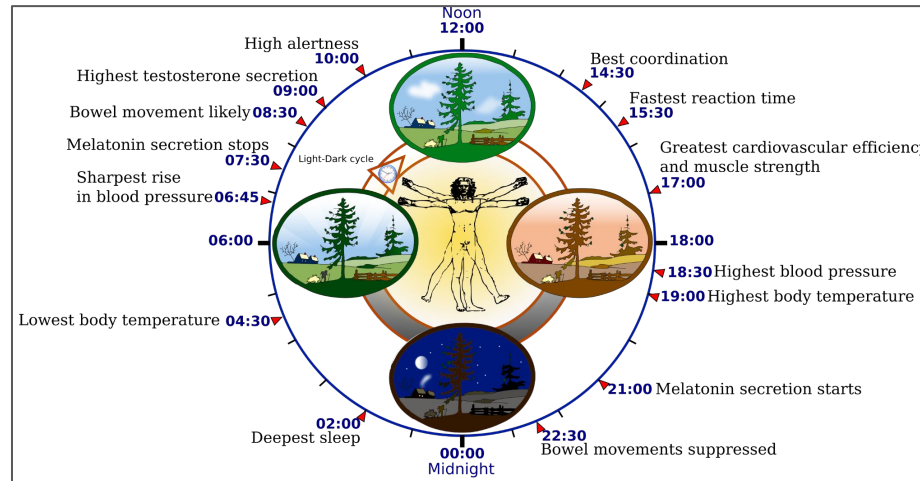
Ruby Kim, University of Michigan



Leloup (2009)



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# Tracing and Forecasting Metabolic Indices of Cancer Patients Using Patient-Specific Deep Learning Models

Jianguo Hou<sup>1,2</sup>, Jun Deng<sup>3</sup>, Chunyan Li<sup>2</sup>, Qi Wang<sup>2</sup>

<sup>1</sup>Beijing Computational Science Research Center, Beijing, China, 100193

<sup>2</sup>Department of Mathematics, University of South Carolina, SC, USA, 29208

<sup>3</sup>Department of Therapeutic Radiology, Yale University School of Medicine, CT, USA, 06520

## Introduction

Digital twin is comprised of three components: the physical (source) product in the physical space, the digital representation of the physical product in the virtual environment, and connections between the two-data and information flowing between the physical and digital products.

### Goal:

- Develop a data-driven, **patient-specific** AI-enabled deep learning model
- To monitor, track, and predict a cancer patient's health states reflected through the metabolic panel from the patient medical records

### Significance:

It is expected to be used by physicians

- To predict the patient's treatment outcome trajectory
- To reduce the treatment-related adverse effects in the short term
- To improve the quality of life of the cancer patient in the long term

## Problem Set Up

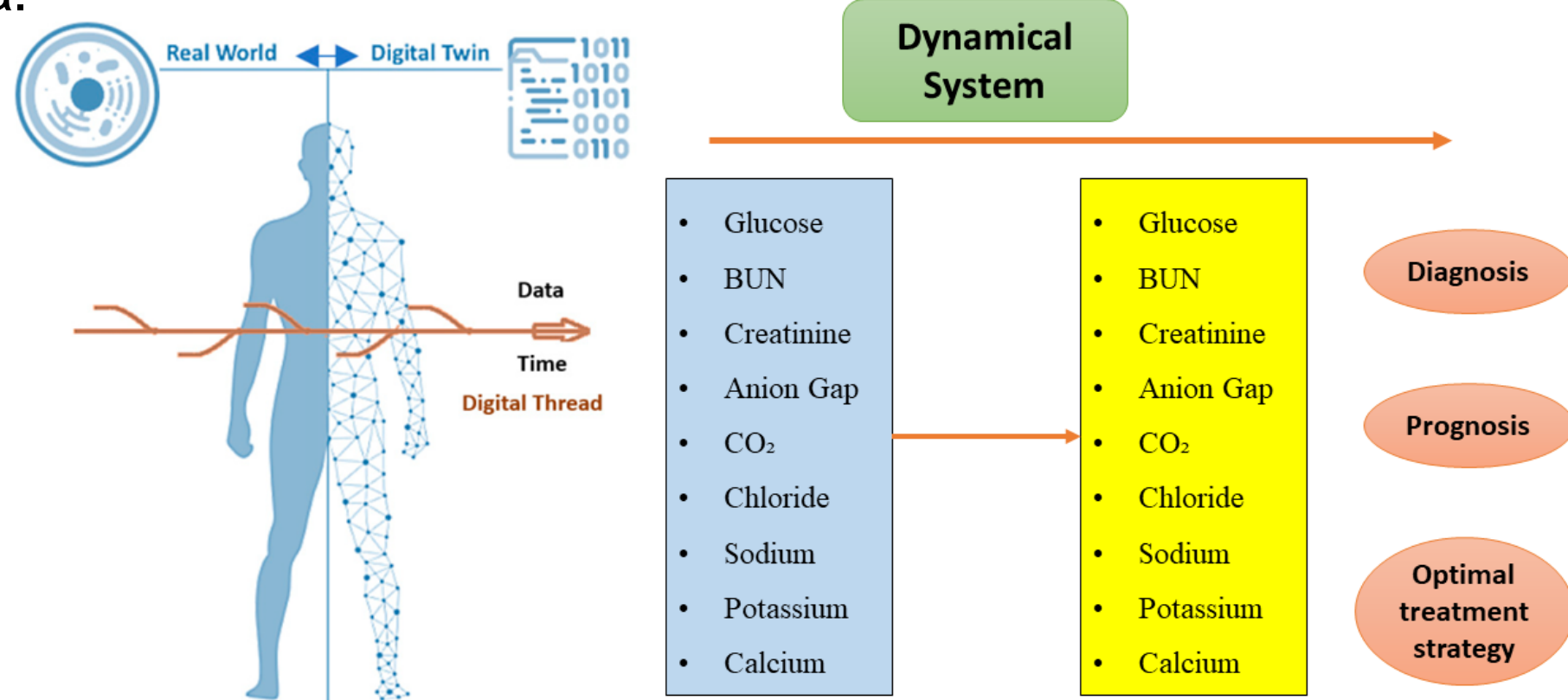
**Question:** For a given time series  $\{x_i\}_{i=1}^n$  how to learn the underlying dynamic system to make predictions for future using neural network?

### Assumption:

- We assume there exists a **self-sustained** dynamical system such as the metabolic system in any human body.
- Any metabolic panel taken from a patient at a given time point would provide a glimpse of the state of the subsystem at that time.
- With **sufficiently** collected time series longitudinal data, one would be able to establish a fairly reasonable dynamical system model to describe the underlying dynamics within the subsystem.

### Idea:

We use the LSTM RNN as the framework to build the patient-specific discrete dynamical system using longitudinal data of the cancer patient's metabolic panel to capture transient dynamics underlying the time series data.



## Model

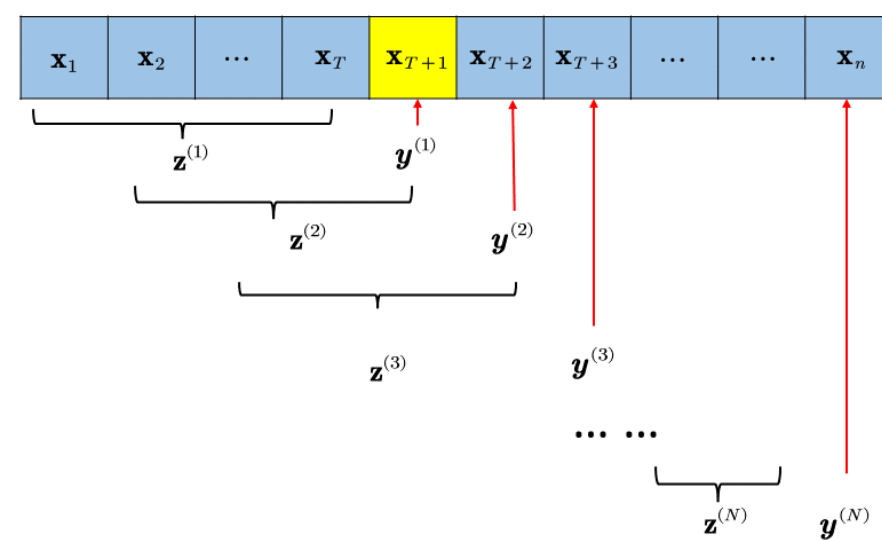
### One-step prediction LSTM model

$$z^{(1)} = [x_1, x_2, \dots, x_T] y^{(1)} = \hat{x}_{T+1},$$

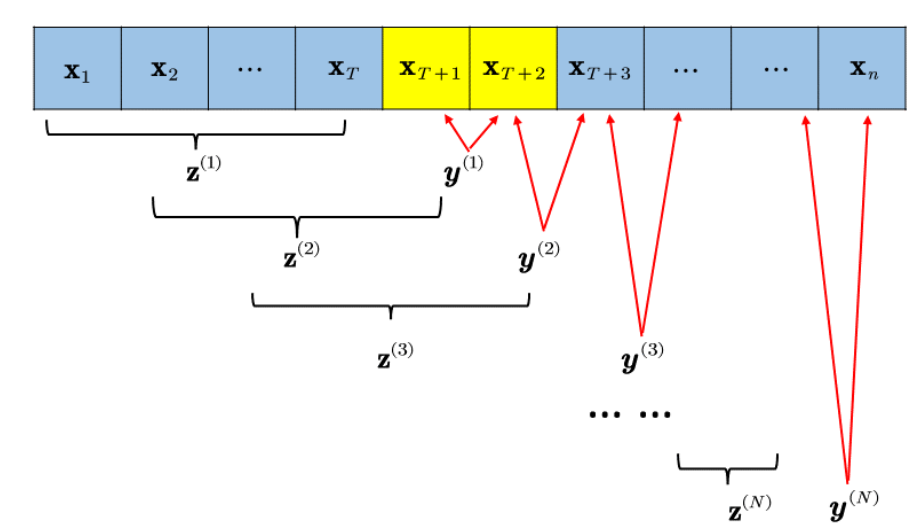
$$z^{(2)} = [x_2, x_3, \dots, x_{T+1}] y^{(2)} = \hat{x}_{T+2},$$

$$z^{(N)} = [x_N, x_{N+1}, \dots, x_{T+N-1}] y^{(N)} = \hat{x}_{T+N}.$$

$$Loss = \frac{1}{N} \sum_{i=1}^N \frac{\|\hat{x}_{T+i} - x_{T+i}\|_2^2}{9}.$$



### Multi-steps prediction LSTM model



$$z^{(1)} = [x_1, x_2, \dots, x_T],$$

$$y^{(1)} = [\hat{x}_{T+1}, \hat{x}_{T+2}, \dots, \hat{x}_{T+L}],$$

$$z^{(2)} = [x_2, x_3, \dots, x_{T+1}],$$

$$y^{(2)} = [\hat{x}_{T+2}, \hat{x}_{T+3}, \dots, \hat{x}_{T+L+1}],$$

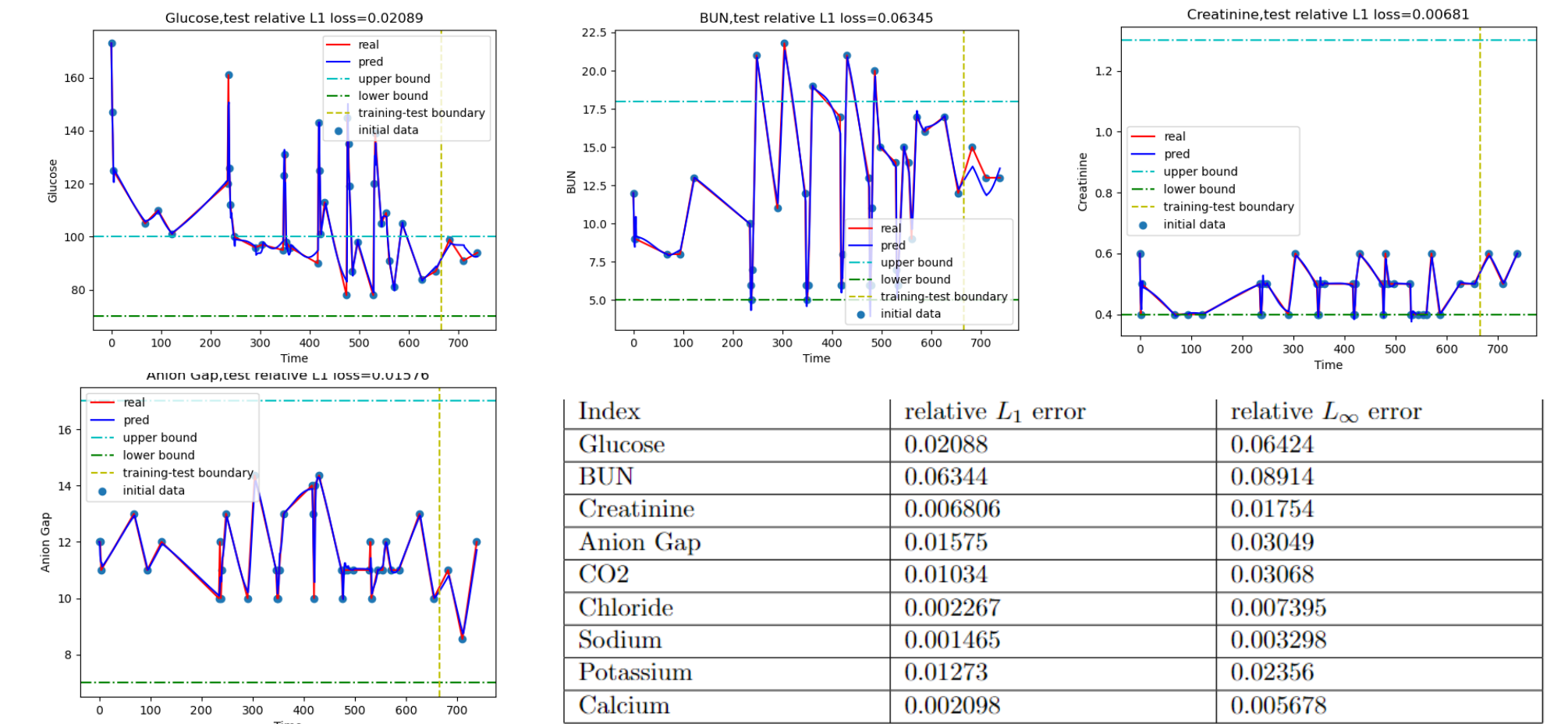
$$\dots$$

$$z^{(N)} = [x_N, x_{N+1}, \dots, x_{T+N-1}],$$

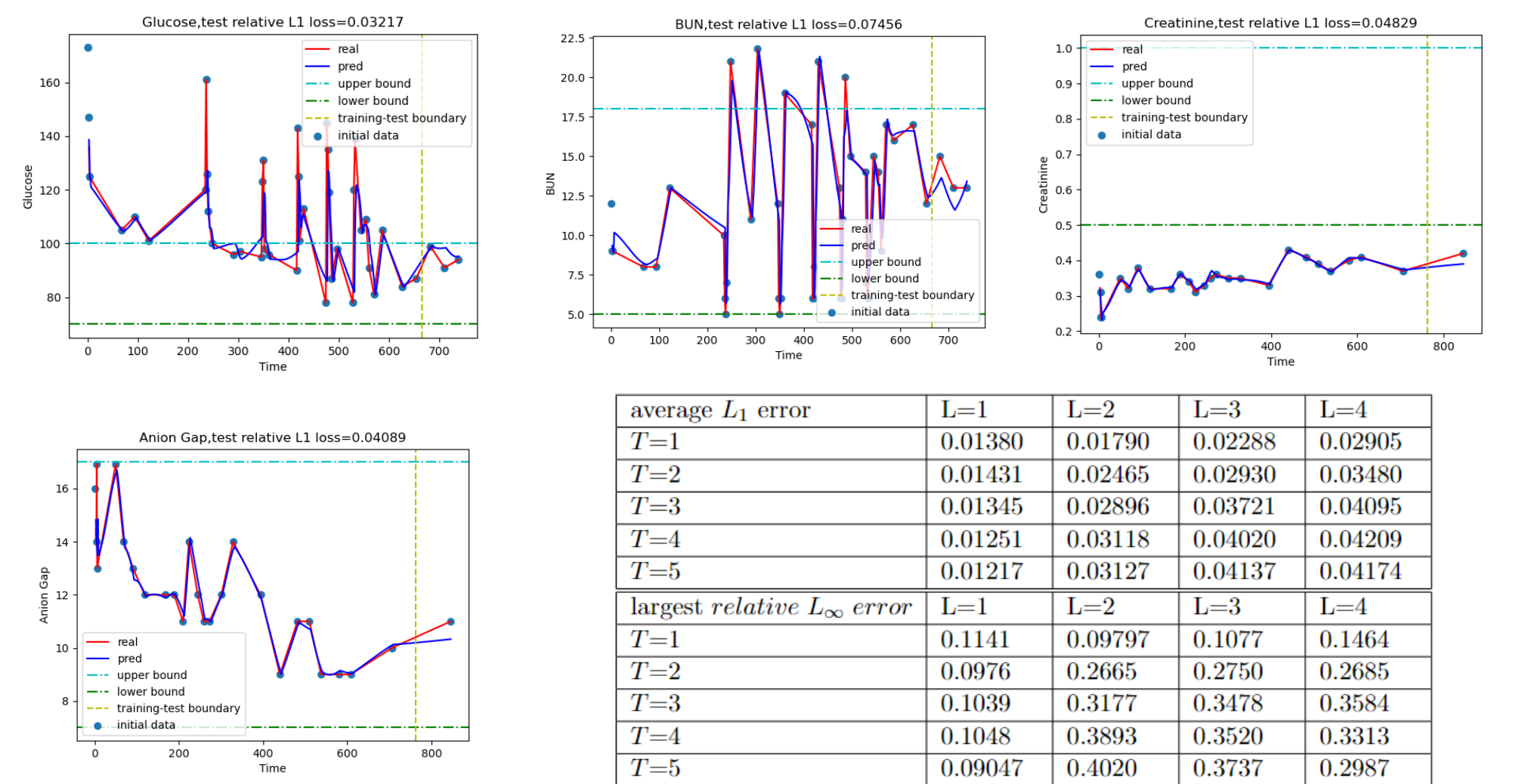
$$y^{(N)} = [\hat{x}_{T+N}, \hat{x}_{T+N+1}, \dots, \hat{x}_{T+N+L-1}].$$

$$Loss = \frac{1}{N} \sum_{l=1}^L \sum_{p=1}^T \frac{\|\hat{x}_{p+l-1+s} - x_{p+l-1+s}\|_2^2}{9 \cdot T}$$

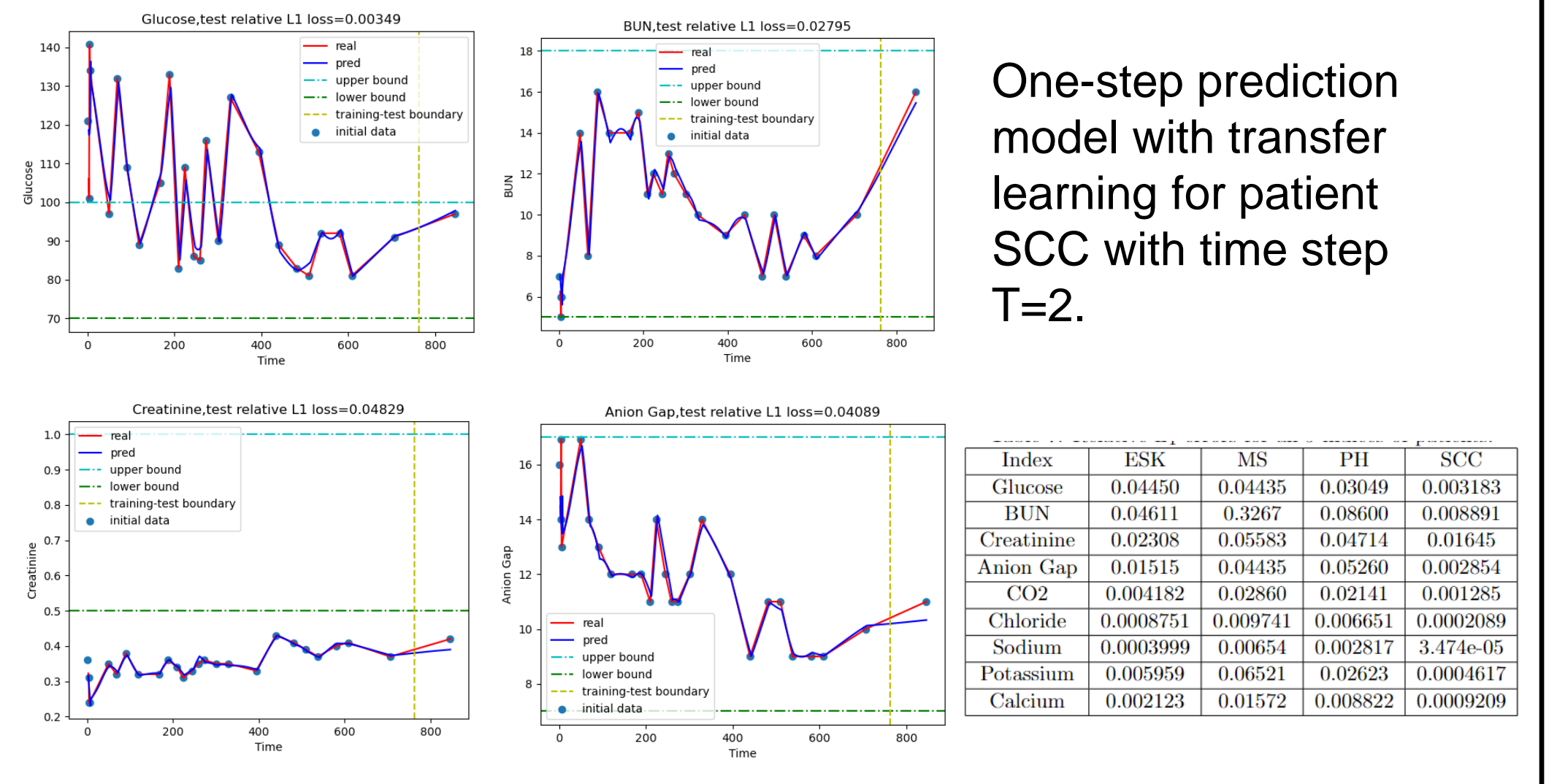
## One-Step Prediction



## Multi-Steps Prediction



## Transfer Learning



One-step prediction model with transfer learning for patient SCC with time step T=2.

## Summary

We have developed a discrete dynamical system model for the metabolic panel of a cancer patient using the LSTM recursive neural network architecture. The patient-specific model can be used to make short term predictions in one step with relative errors consistently less than 10% in the absolute value and much less than it in an average sense. It can be applied to make multi-step predictions with a slightly elevated error level (i.e., relative error less than 11% in three steps and 15% in four steps). Using four additional cancer patients' metabolic panel, we show that the patient specific LSTM model can be calibrated through transfer learning to other cancer patients. This modeling platform has a great potential in shaping digital twin models for cancer patients.

### Publication

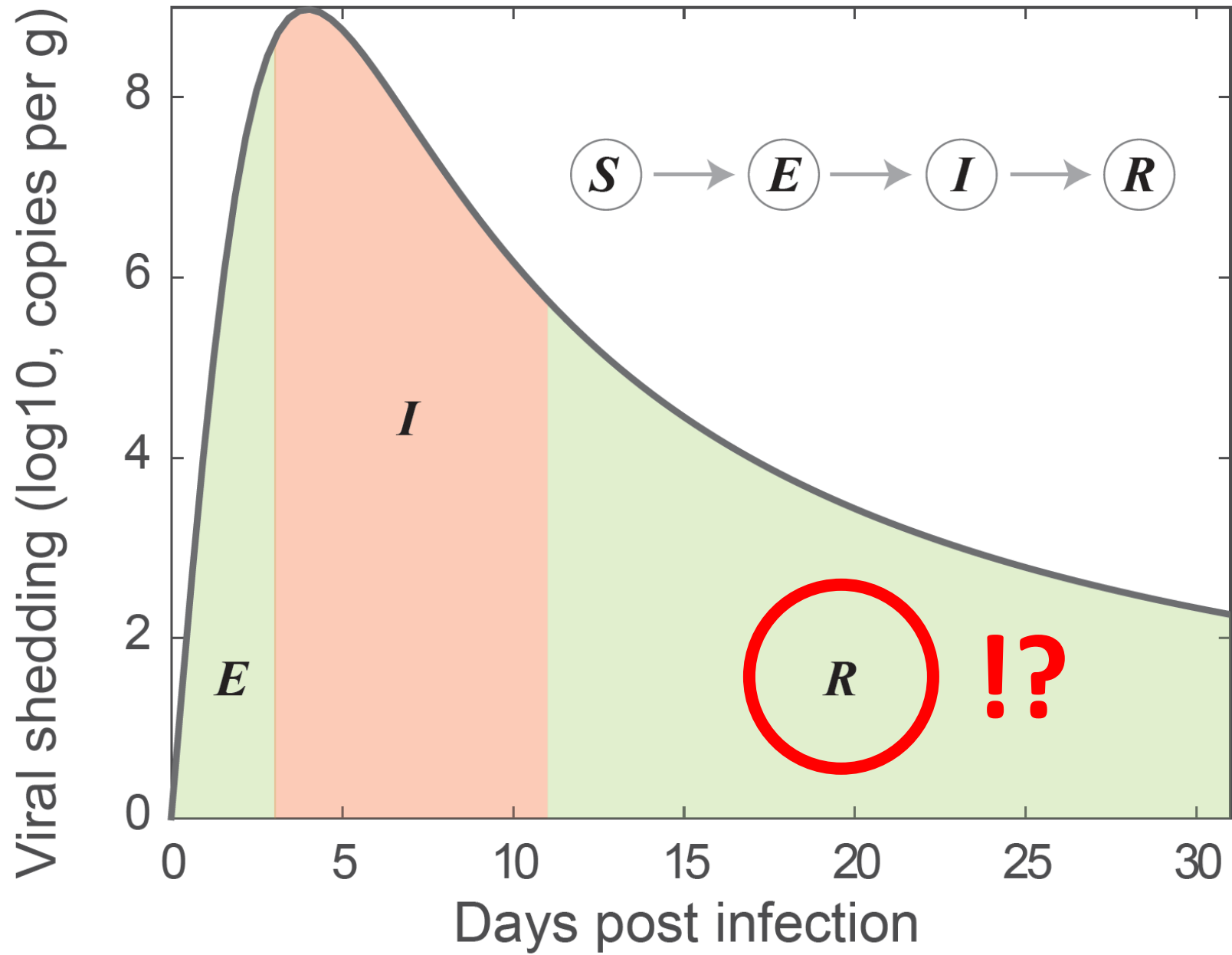
Hou, Jianguo, Jun Deng, Chunyan Li, and Qi Wang. "Tracing and forecasting metabolic indices of cancer patients using patient-specific deep learning models." *Journal of personalized medicine* 12, no. 5 (2022): 742.



# **Prolonged viral shedding from noninfectious individuals confounds wastewater-based epidemiology**

**Tin Phan – Los Alamos National Laboratory**

**ICERM – Mathematical and Computational Biology**



# Machine learning-assisted protein engineering

Yuchi Qiu

Department of Mathematics,  
Michigan State University



**MICHIGAN STATE**  

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**UNIVERSITY**



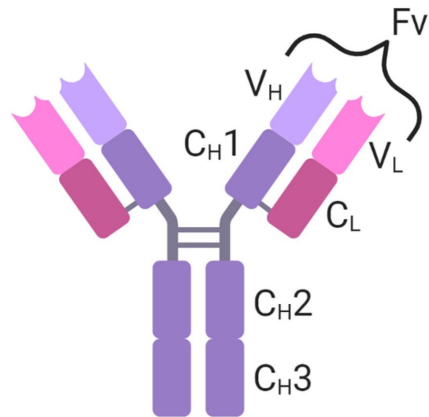
# Machine learning for protein engineering

## Protein engineering

optimizes protein and its functions.

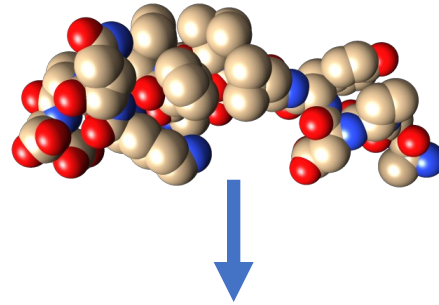
### Applications:

- Agriculture
- Pharmaceutical
- Etc.



**Step 1:** predict protein function

### TopFit



Protein functions?

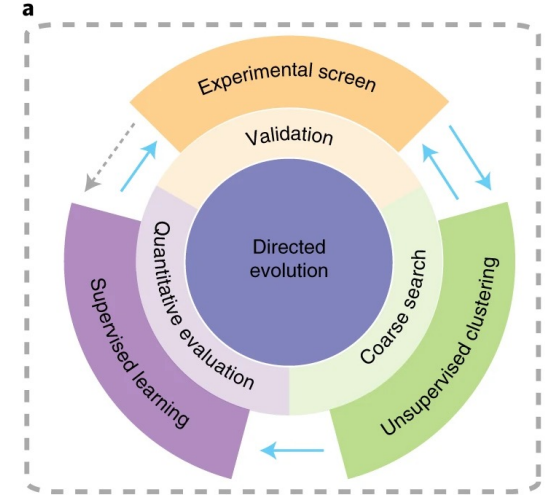
- Deep protein language models (e.g., **Transformer**)
- New **topological data analysis** method (persistent spectral Laplacian)

*Nature Computational Science, 2023*

**Step 2:** optimize protein function

### CLADE

$$x^* = \arg \max_a f(x),$$



Deep/machine learning

- NLP models
- Zero-shot strategy
- Unsupervised clustering
- Ensemble regression

*Nature Computational Science, 2021*

# An Efficient Finite Element Solver for a Nonuniform Size-modified Poisson-Nernst-Planck Ion Channel Model

Dr. Dexuan Xie

Department of Mathematical Sciences  
University of Wisconsin-Milwaukee

## Acknowledgments:

- National Science Foundation through DMS-2153376.
- Simons Foundation through research award 711776.

## Abstract

This poster presents an efficient finite element solver for computing a linear finite element solution of a nonuniform size-modified Poisson-Nernst-Planck ion channel model, denoted by SMPNPIC. It includes a damped iterative method and a software package workable for an ion channel protein crystallographic structure and an ionic solution with multiple species. In particular, mathematical transformation, decomposition, and iteration techniques are developed such that a SMPNPIC finite element solution can be found by only solving linear boundary value problems and nonlinear algebraic systems, totally avoiding the numerical difficulties caused by the strong nonlinearities, un-symmetric forms, and singularity of SMPNPIC. Numerical results for a voltage-dependent anion channel (VDAC) and a mixture of four ionic species demonstrate the convergence and performance of the damped iterative method.

## Size-modified Nernst-Planck equations in steady state

$$\nabla \cdot \mathcal{D}_i \left[ \nabla c_i(\mathbf{r}) + Z_i c_i(\mathbf{r}) \nabla u(\mathbf{r}) + \frac{v_i}{v_0} c_i(\mathbf{r}) \frac{\gamma \sum_{j=1}^n v_j \nabla c_j(\mathbf{r})}{1 - \gamma \sum_{j=1}^n v_j c_j(\mathbf{r})} \right] = 0, \quad \mathbf{r} \in D_s, \quad i = 1, 2, \dots, n,$$

which is reduced to the classic Nernst-Planck equations:

$$\nabla \cdot \mathcal{D}_i [\nabla c_i(\mathbf{r}) + Z_i c_i(\mathbf{r}) \nabla u(\mathbf{r})] = 0, \quad \mathbf{r} \in D_s, \quad i = 1, 2, \dots, n,$$

Is strongly coupled together, making them difficult to solve numerically.

We overcome this difficulty by developing techniques of **mathematical transformation**,  
**function decomposition**, and **numerical iteration**

so that we can get a numerical solution by only solving

**linear boundary value problems**,

plus **a system of nonlinear algebraic equations!**