Systems Biology and Artificial Intelligence
University of Udine, School of Medicine

Dates: Weekdays Monday March 4th-15th Approximately 9:00 am-5:00 pm

Instructor: Tinen Iles, PhD, University of Minnesota Department of Surgery -guest lecturers

Pre-course activities: Please complete the survey by February 12th

Books, Texts and Papers: (all books will be available and copies of papers provided)

A First Course in Systems Biology- Voit, Eberhard

The Hundred-Page Machine Learning Book-Burkov, Andriy

Neuromorphic Engineering- Tsur

Computer Vision in Medical Imaging, CH Chen

The AI Revolution in Medicine: GPT-4 and Beyond, Lee, Peter

R for Excel Users: An Introduction to R for Excel Analysts, Taveras, John L

R Programming For Beginners: How To Program In R And How To Use R For Effective Data Analysis- Majersky, Fausto

Section 1: Fundamentals of Systems Biology (Monday-Wednesday)

<u>Monday March 4:</u>

9:00-9:45 am: Course introduction (Iles): Overview of the class and resources

9:45-10:30 am: Ideation activity (Iles): Ideation and Ice Breaker activity " My Fancy Computer can do This.."

10:30-11:00 am: Break and Discussion

11:00-12:00: Introduction to the theory of systems biology (Iles) Introduction to the the course and paradigm of systems (gene, protein, metabolic, signaling and population systems)

12:00-1:00 Lunch

1:00-2:00 pm: Introduction to Mathematical Modeling (Iles) Introduction to the utility of computational tools to solve problems and prediction in physiology and medicine

2:00-3:00 pm: <u>Adventures in Multi-Modal Data: from innovation to application (Iles): Open Seminar</u> A brief history of my journey in science, research and perspective on using multi-modal in computational modeling from understanding biological mechanism to patient care

3:00-3:30 pm: Break and Discussion

3:30-5:00 pm: Introduction to Programming in R (Sham): Introduction to programming and how it can be used to solve problems in systems biology and AI, assignment

<u>Tuesday March 5th:</u>

9:00-10:30 am: Introduction to Molecular Structure (Sham): Introduction to molecular systems and the computational tools that can be used to predict and experiment in molecular systems

10:30-11:00 pm: Coffee break and Discussion

11:00-12:00 pm: Physiological and Multi-physics modeling: Heart as an Example (Iles) Introduction to the concepts and tools to model whole physiological systems and cardiac applications (highly applicable to clinicians and translational scientists)

12:00-1:00 pm: Lunch

1:00-2:00 Introduction to Dynamic Biochemical Systems and Kinetic Models of Biochemical Networks (Sham): Overview of the methods and examples of biochemical modeling, analysis of systems dynamics, limit cycles and chaotic attractors and introduction to discrete/stochastic models

2:00-3:00 pm Literature Review (Iles/Sham) Small group review of literature with provided papers or others of interest, review the emerging topic and prepare a short review of the methods and what is solved in systems biology (for Wed. am)

2:30-3:00 Coffee break and Discussion

3:00-4:00 pm: Group activity on kinetic modeling (Sham) Systems biology chemical equilibrium in a feedback system, to plot concentration and temporal resolution- code provided

4:00-5:00 pm: Introduction the Metabolic Systems (Lusczek): Further introduce rate laws, biochemistry, detection, sampling, extraction, flux analysis, and resources for computational pathway analysis and examples of applied research ==(highly applicable to clinicians and translational scientists)==

<u>Wednesday March 6th:</u>

9:00-10:30 am: Introduction to Protein Systems (Cantarutti): Further introduce chemical and physical features of proteins, enzymes, transporters, carriers, signaling, messengers, structure function and prediction

10:30-11:00 am: coffee break

11:00-12:00 pm: Review of Literature, Emerging Topics, Case Studies (Iles/Sham): Small groups will provide a short synopsis of the literature they reviewed, we will discuss as a group and provide case studies

12:00-1:00 pm: Lunch

1:00-2:00 pm: Prediction in Protein folding (Sham): ==TBD==

2:00-3:00 pm: Introduction to Gene Systems: Evolution and Optimality (Drabeck): Introduction to evolution, selection, types of selection, mathematical models that will lead into an interactive activity in the afternoon session

3:00-5:00 pm: Hands-on Activity (Drabeck): This activity will work a genome dataset from the previous lecture

Section 2: Tools in Machine Learning/Artificial Intelligence/Numerical Methods and Simulation (Thursday-Monday)

<u>Thursday March 7th</u>

9:00-10:00 am: Introduction to Artificial Intelligence (Iles): Introduction to AI and theory of AI and integration of how we can capture the power of AI for research in systems biology and research in medicine

10:00-10:45 am: Introduction to Machine Learning Part 1 (Iles): Introduction to machine learning, notation and definitions, fundamental algorithms, best practices, neural networks and deep learning

10:45-11:00 am: Break and Discussion

11:00-12:00 am: Introduction to Machine Learning Part 2 (Iles): Introduction to machine learning, problems and solutions, advanced practice, unsupervised learning and other forms of learning

12:00-1:00 pm: Lunch

1:00-2:00 pm: Prediction of Protein Structure with AlphaFold (Corazza/Iles) Discussion of protein folding and the utility of emerging computational methods to predict protein structure with atomic accuracy

2:00-3:00 pm: Introduction to Natural Language Processing (Zhang) Introduction to modeling NLP and how this work can be applied in multi-omics data, especially related to the health informatics<mark>(highly applicable to clinicians and translational scientists)</mark>

3:00-5:00 pm: "Cocktail napkin" Reflection/Free time How can I use AI/ML? Bring your questions in the morning!

<u>**Friday March 8th**</u>

9:00-10:00 am: How do I use a supercomputer? (Iles) Introduction to computational tools that are available, what type of performance is needed for different data types and how to access them

10:00-11:30 am: Population Systems and AI applied to databases (Lassen) Deeper dive into practical examples of population systems biology and the tools that are used to extract data and identify health care trends with the use of AI, why is the use of AI appealing in this setting? History of building database systems in healthcare in a country, what do you get out of it? Systems of mining the data; AI in deeper learning and discussion (Iles/Lassen) what are the problems for black box systems<mark>(highly applicable to clinicians and translational scientists)</mark>

11:30-1:00 pm: Lunch and Discussion

1:00- 2:00 pm: Clinical Imaging: computer vision and segmentation using AI (Iles) Introduction to AI/ML in the use of clinical imaging and how we can use tools in AI for

3D/4D data and segmentation and basic ways that we can observe accuracy such as dice scores (highly applicable to clinicians and translational scientists)

2:00-3:00 pm: Introduction Applications workshop activities and presentations for next week (Iles)

3:00-5:00 pm: Free time to get started on research

<u>Monday March 11th</u>

Academic/Industry Lectures

9:00-9:30 am: Review of the Data and Research Question for Ideation Sessions (Iles)

10:00-11:00 am: Multi-physics Modeling of Cardiac Function (Aguado-Sierre) Dr. Jazmin Aguado-Sierre will share her expertise in High-Performance Modeling, pre-exascale and exascale computing from electrophysiology to *in silico* trials to Digital Twins and her work with the Barcelona Supercomputing Center and ELEM Biotech(highly applicable to clinicians and translational scientists)

10:30-11:00 am: Break and Discussion

11:00 am- 12:00 pm: Journey of Healthcare to Changing Outcomes (Lassen) Prof. Jens F Lassen will share his journey of transforming outcomes for out of hospital cardiac arrest leveraging AI and Danish Heart Registry and National Databases (highly applicable to clinicians and translational scientists)

12:00 pm- 1:00 pm: Lunch

1:00-2:00pm: AI Revolution in Medicine and Code using ChatGPT (Iles) Introduction to perspective related to medicine and the augmentation of patients and challenges for using AI in medicine (highly applicable to clinicians and translational scientists)

2:00-2:30 pm: Break and Discussion

2:30-3:00 pm: Ethics in Artificial Intelligence (Fitzpatrick?) Introduction to emerging considerations for utilizing AI/generative AI for the creation of academic work and research

3:00-4:30 pm: Explainable Artificial Intelligence (Pedersen) Dr. Lykke Pedersen will share her research in predictive modeling with the use of explainable artificial intelligence and her industrial work at Abzu

Section 3: Application Workshop and Presentations (Tuesday-Friday)

Tuesday March 12th

9:00-10:00 am: Ideation Exercise and Presentation Preparation 1 - _Emphathize_ (Iles/independent group work) Revisiting our ideation session from last week, we will work through a process for ideation. Empathize: by first developing a deep understanding of the problem

10:00- 11:00 am: Ideation Exercise and Presentation Preparation 2 - _Define_ (Iles/independent group work) Clearly articulate the problem you would like to solve

11:00am- 12:00 pm: Ideation Exercise and Presentation Preparation 3 – _Ideation_ (Iles/independent group work) Brainstorm potential solutions using AI/ML and computing and develop your ideas

12:00-1:00 Lunch

1:00-2:00 pm: Biomimetic and Translational Research in the Black Bear: explainability of adaptation in biological systems (Iles): Review of black bear research and applications of explainable AI looking at adaptations of bears during long periods of hibernation and immobility (highly applicable to clinicians and translational scientists)

2:00- 5:00 pm: Ideation Exercise and Presentation Preparation 4 – _Prototype_ (Iles/independent group work) Design a prototype with what you have learned and researched about the tools in systems biology, AI, ML, this does not need to be a working prototype, but could be!

Wednesday March 13th

9:00-10:00 am: Validation, Verification and Uncertainty Quantification: the use of simulation and software as a medical device (SaMD) (Iles): Introduction to the VVUQ process of validating medical devices and software used as a medical device for clinical decision making and an example of an end-to-end industrial example and physiological high-performance computing (highly applicable to clinicians and translational scientists)

10:00- 12:00 pm: Ideation Exercise and Presentation Preparation 4 – _Test_ (Iles/ independent group work) Review your ideation process so far, and with the considerations of the VVUQ process, suggest how you would test your prototype and regulate for safety, accuracy etc.

12:00-1:00 Lunch

1:00- 2:00 pm:

2:00- 5:00 pm: Presentation Preparation and Group Discussions (Iles/ independent group work)

Thursday March 14th

9:00-10:30 am: Presentations for group 1 and Discussion

10:30-11:00 am: Break and Discussion

11:00-12:30 pm: Presentation group 2 and discussion

12:30-1:30 pm: Lunch

1:30-3:00 pm: Presentation 3 and discussion

3:00-3:30 pm: Break and Discussion

3:30-5:00 Presentation 4 and discussion

Friday March 15th

9:00-10:30: Presentations for group 5 and discussion

10:30-11:00 am: Break and Discussion

11:00-12:30 Presentation group 6 and discussion

12:30-2:00 pm: Lunch

2:00-3:30 Presentation 7 and discussion

3:30-4:00: Course conclusion and available resources