Del and Beth Kimbler Lecture Series
@Industrial and Management Systems Engineering

Evolutionary Therapy

Alexander R.A. Anderson

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Biography

Alexander R. A. Anderson, PhD is Founding Richard O. Jacobson Chair of the Integrated Mathematical Oncology (IMO) Department and Director of the Center of Excellence for Evolutionary Therapy at Moffitt Cancer Center. For the last 20 years he has been developing mathematical models of many different aspects of tumor progression and treatment that require a tight dialogue between theory and experiment. Due to his belief in the crucial role of mathematical models in cancer research he moved his group to the Moffitt Cancer Center in 2008 to establish the IMO department. Since his arrival, cancer treatment has become a significant driver of his research and using mathematical models that connect our basic science understanding of a given cancer with clinical translation. This has led to the development of evolutionary therapies that seek to control cancer rather than eradicate it. Through smart treatment scheduling and dosing, with combination therapies as well as microenvironment targeted treatments, he has developed novel treatments for prostate, breast, ovarian, lung and skin cancer. As director for the 1st center of Evolutionary Therapy he has helped facilitate 8 active evolutionary clinical trials at Moffitt that use mathematical models as part of their decision process. One of these trails is the Evolutionary Tumor Board (ETB), which consists of an integrated team of clinical physicians, evolutionary biologists, and mathematicians. The ETB provides guidance on optimal evolution based treatment strategies for individual patients by rigorously formulating and

CMC 147
11:00am-12:30pm
Friday, September 1, 2023

Abstract

Our current approach to cancer treatment has been largely driven by finding molecular targets, those patients fortunate enough to have a targetable mutation will receive a fixed treatment schedule designed to deliver the maximum tolerated dose (MTD). Cancers are complex evolving systems that adapt to therapeutic intervention through a suite of resistance mechanisms, therefore whilst MTD therapies generally achieve impressive short-term responses, they unfortunately give way to treatment resistance and tumor relapse. The importance of evolution during both tumor progression, metastasis and treatment response is becoming more widely accepted. However, MTD treatment strategies continue to dominate the precision oncology landscape. Here we discuss evolutionary therapy, a proactive therapeutic approach that changes and evolves with the tumor being treated. Due to the dynamic feedback between changing treatments and the evolving tumor, mathematical models are essential to drive treatment switch points and predict appropriate dosing and drug combinations. We will consider the importance of using treatment response as a critical driver of subsequent treatment decisions, rather than fixed MTD strategies that ignore it. We will also consider using mathematical models to drive treatment decisions based on limited clinical data. Through the integrated application of mathematical and experimental models as well as clinical data we will illustrate that, evolutionary therapy can drive either tumor control or extinction. Our results strongly indicate that the future of precision medicine shouldn't only be in the development of new drugs but rather in the smarter evolutionary, and model informed, application of preexisting ones.

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A provably stable neural network Turing Machine-Towards Trustworthy AI

Assistant Professor in the Department of Computer Science and Engineering at the University of South Florida (USF)

Biography

Dr. Ankur Mali is an assistant professor in the Department of computer science and Engineering at the University of South Florida (USF), where he directs the trustworthy knowledge drive artificial intelligence (TKAI) laboratory. Before joining USF, he completed his Ph.D. under Prof. Clyde Lee Giles from The Pennsylvania State University in 2022. He works at the intersection of language, memory, and computation—spanning Natural Language Processing (NLP), linguistics, and formal language theory. He also works on designing learning algorithms and computational architectures guided by theories of the brain. These architectures focus on solving challenges such as continual/lifelong learning, learning with minimal supervision, RL, and sparsity (both in computer vision and natural language processing). In particular, he has proposed several knowledge-guided interpretable deep learning systems that generate fair, accountable, and trustworthy information. Furthermore, he has also designed approaches to investigate the mysterious success of deep learning in recognizing natural language from a theoretical and empirical perspective.

Abstract

Artificial intelligence's remarkable advancement, especially deep learning-based intelligent systems, has achieved human-level performance in various domains. Although state-of-the-art (SOTA) Neural networks (NNs) such as recurrent neural networks (RNNs) and transformers are known to be Turing-complete, this result relies on infinite precision in the hidden representation, positional encoding for transformer models, and unbounded computation time. Furthermore, there needs to be a more theoretical understanding of the mysterious success of these black-box systems under constrained resources.

In this talk, I will draw a connection between formal methods, linguistic theory, and Neural network architectures and show the theoretical limits of modern-day NNs. Later I will show how one can extract and insert rules in this black-box system, such that the underline system is explainable by design and extraction. Furthermore, I will talk about our recent theoretical work in constructing the smallest NN that can simulate a Turing Machine in real time with bounded precision in weights. Finally, using orbital stability, we show that solutions built by our models are always stable, which is a crucial step in designing robust, stable neuro-symbolic models that can generalize to unseen distribution.

ENC 2004
11:00am-12:15pm
Monday, April 17th, 2023

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