Abstract

Personalized medicine requires the right interventions for the right patient at the right time. This necessitates parsing individual patient trajectories at a mechanistically relevant temporal resolution, a task for which existing biomedical data sets are inadequate. High-performance computational modeling and simulation can help dynamically contextualize multi-dimensional data arising from complex systems; however, knowledge of the mechanics of a complex system does not directly lead to the understanding of how to alter these mechanics to a specific end. In this study, we examine and assess the efficacy of using evolutionary algorithms to develop control strategies for a stochastic dynamical immune system.

Methods

Genetic Algorithm:
- Efficiently search a large parameter space using evolutionary principles
- 4 inhibition strengths, 4 augmentation strengths, 300 billion combinations/sequential intervention, $10^{91}$ for 8 sequential interventions
- Run simulation with intervention
- Test intervention for “fitness” – how well did it perform
- Top 50% fittest individuals breed, chance for mutation
- Repeat until convergence to small set of solutions
- GA trained on 1 individual, RNG was reseeded at start of intervention

A: single parameter set, 100 stochastic replicates; B: single parameter set, single individual, reseed at intervention start

Extreme-scale Model Exploration With Swift (EMEWS) Workflow

EMEWS combines existing machine learning/model exploration libraries (i.e., DEAP – Distributed Evolutionary Algorithms in Python) with the Swift/T parallel scripting language to run scientific workflows in an HPC environment. This work was performed on Midway at the RCC and Beagle at the CI, an utilized up to 2000 processing cores simultaneously.

Results

- GA-derived intervention significantly reduces mortality rate in training set and generalizes well to several Alternate Parameter Sets
- Poor performance on Alternate Parameter Set 3 due to fixed-length interventions and inability to adapt to non-responders in real-time

Discussion

- Stochastic, chaotic dynamical immune system is controllable
- Calculated interventions are generalizable
- Personalized interventions are necessary to increase level of success
- GA uses too many fixed parameters (intervention length, number of interventions in sequence), alternate machine learning techniques may be more efficient (e.g., deep reinforcement learning)

Alternate Treatment for Intervention Non-Responders

This patient exhibits an enhanced response to GCSF stimulation
- New GA experiment upon significant deviation from the average response leads to personalized intervention sequence, saves non-responder
- Original intervention is shown on the left; Alternate intervention sequence shown on right

References