A Model System for Study of Cyberattacks on Biomanufacturing

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BACKGROUND

- Cyberattacks: a major concern for biological systems and healthcare networks
- Healthcare cyberattacks make up 25% of all hacks, and each one costs avg. $5 million (Nature, 2022)
- We designed a model bioreactor to study cyberattacks in biomanufacturing
- The reactor improves the efficiency of immunotherapy, a promising but expensive new cancer treatment
- The centrifugal bioreactor (CBR), Figure 1, balances fluid and centrifugal forces (Figure 2) to quickly grow killer T cells up to high density
- We have designed models to automate the process and account for effects of cyberattacks and interruptions
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METHODS & RESULTS

Kinetic Modeling

- Glucose and oxygen: key nutrients for T cells. We optimized cell growth in the CBR using the following model:

\[
\frac{dC_{cell}}{dt} = \mu_{max} \left( 1 - \frac{C_L}{C_{L,max}} \right)^n \left( 1 - \frac{C_A}{C_{A,max}} \right)^m \cdot C_{cell}
\]

- Current CBR prototype with centrifuge chamber visible in the center
- Kinetic studies were performed in lab to measure each term in model. Results of modeling are shown below in Figure 3
- Model calculates cell growth (equation 1) as function of glucose (equation 2), ammonium and lactate (toxic byproducts, equations 3, 4), additionally oxygen (not shown)
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- Semi-log graph showing normalized glucose concentration against time in hours

Cyberattack Modeling and Prevention

- Our planned process, shown in Figure 4, will:
  - Collect glucose/oxygen data from sensors, send it to Simulink, compare real data to model
  - Use Arduino controllers to make adjustments
  - Current process flow: software run through a browser (DOTS by SBI), with data sent to an Excel sheet in real time to compare reactor data to model predictions
  - Web browser makes system vulnerable to online attacks, as browsers on either side could be hacked, shown by red line (untrusted source)

Automated Data Acquisition

- We designed a script:
  - Automatically logs into oxygen sensor software, downloads/overwrites current CBR data, locally updating while CBR runs
  - Uses Python and its libraries, such as Pandas and Selenium.
  - Has applications for tracking local data compared to online data to maintain records, ensuring data validity

FUTURE WORK

- Further develop model and automated data collection system
- Goal: design process controllers that adjust key conditions (glucose/oxygen) in response to interruptions and hacks to the process

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- Figure 5: Script in Python which automates data collection
- Figure 4: Overview of the reactor process and cybersecurity risks
- Figure 3: Model predictions of cell growth over 250 hours
- Figure 1: Current CBR prototype with centrifuge chamber visible in the center
- Figure 2: CBR chamber on top of centrifuge disc; balance of forces on each cell within the chamber

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Figure 3: Model predictions of cell growth over 250 hours

Figure 4: Overview of the reactor process and cybersecurity risks

Figure 5: Script in Python which automates data collection