Cybersecurity In Biological Systems

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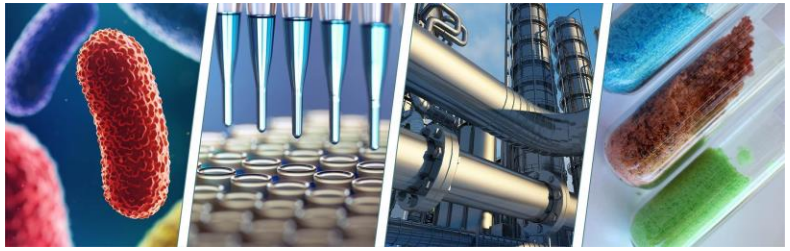
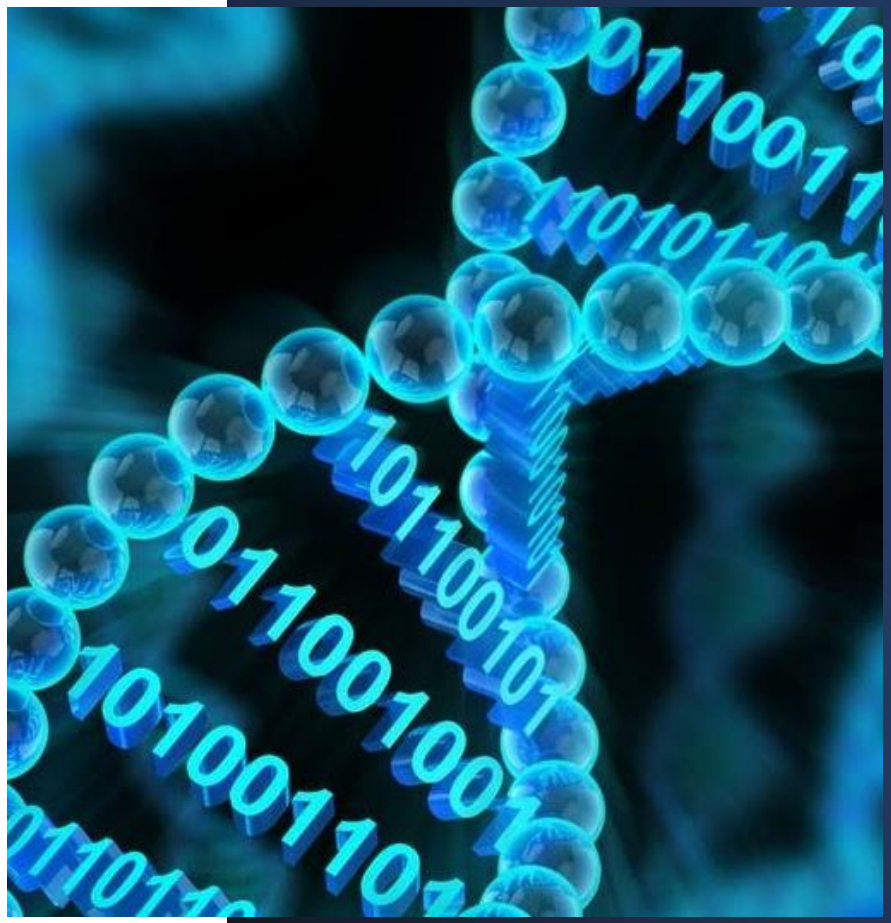
Biomanufacturing

- Biological systems (cells, tissues) → valuable products
  - **BIOREACTORS**
- 2020: ~$19B market
  - $85B market by 2031 (annual growth rate of 15%)
- Addresses many future issues
  - Medicine/health
  - Water/food security
  - Sustainable energy



Cybersecurity implications in biotech

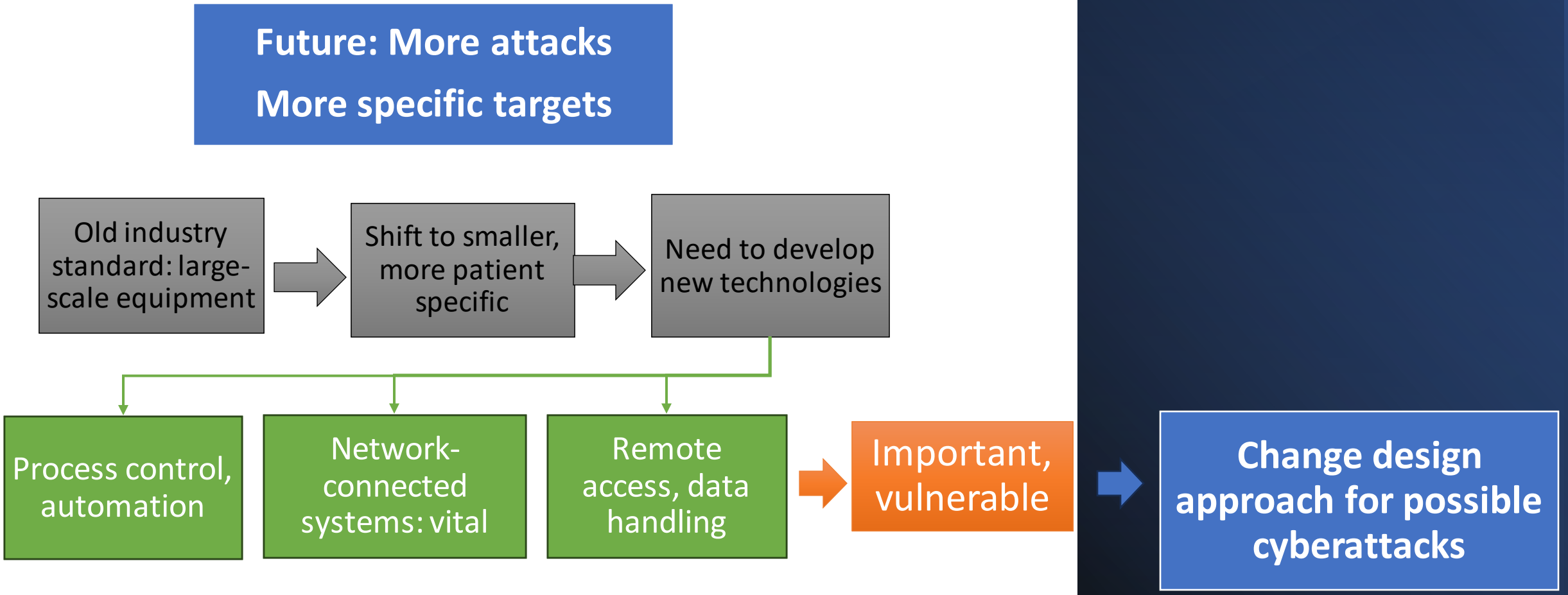
- Many stakeholders: **healthcare, government, industry**
- Interruptions to global production, pandemic response
- Sensitive medical data
  - Data breaches in healthcare: up 10% each year 2010-2019
- Recent sabotage, IP theft, extortion attempts on systems in biotech



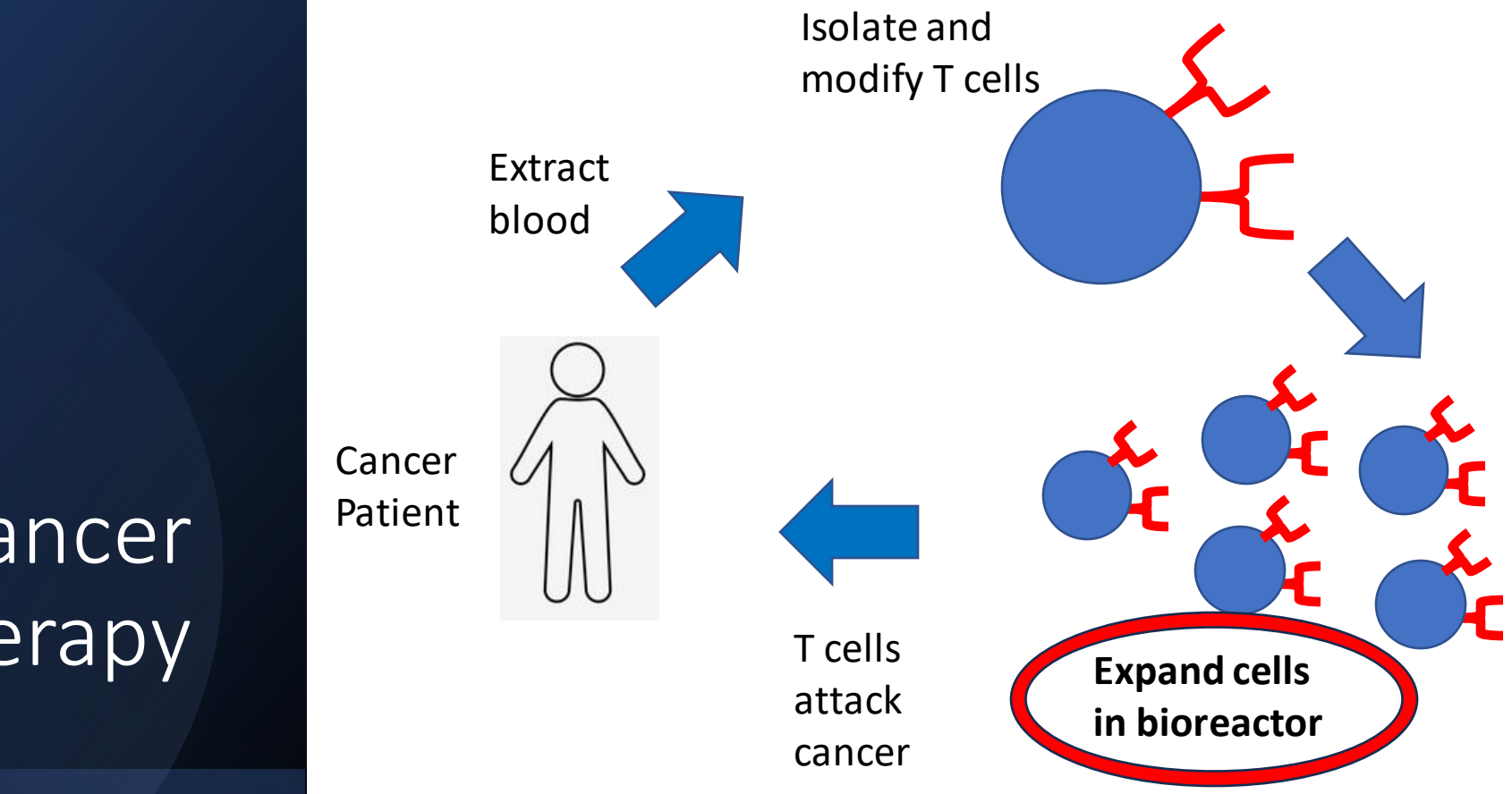
Example: Merck & Co, 2017

- Modified ransomware worm: encrypted data on computer systems
  - Affected manufacturing
  - Vaccine shortages, Merck had to borrow from CDC
- Total cost of attack: ~$1 billion
- No evidence that Merck was targeted
  - US/UK attributed attack to Russia

Next Gen Biomanufacturing



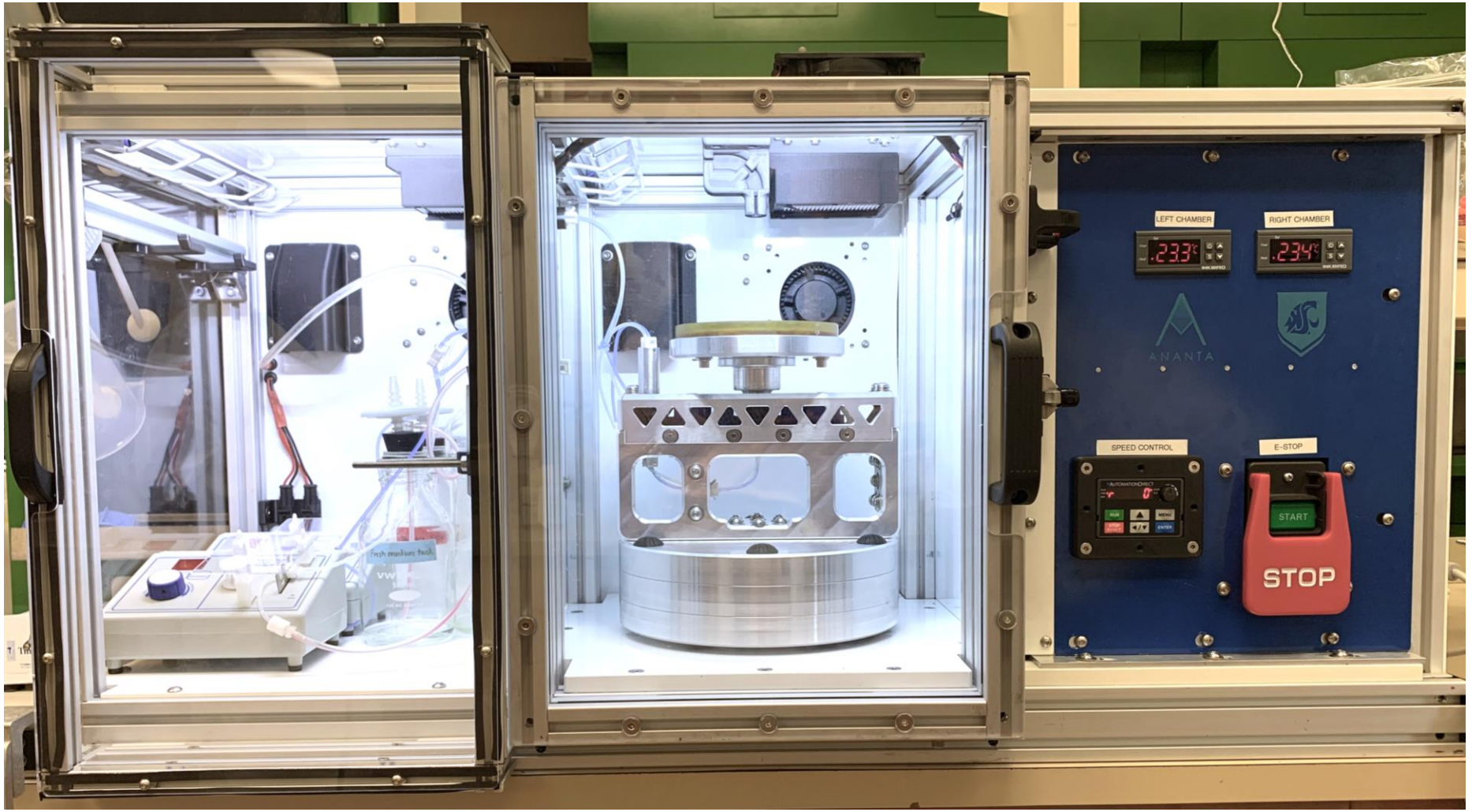
Cancer Immunotherapy



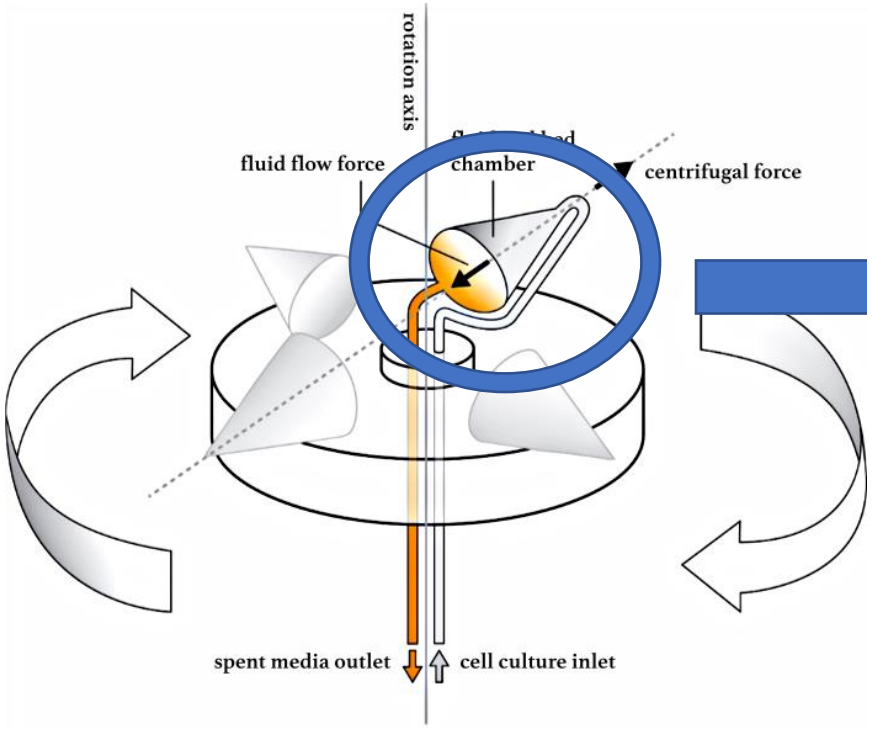
GOOD: healthy cells (vs. chemo etc.), **patient specific**, process customization/automation

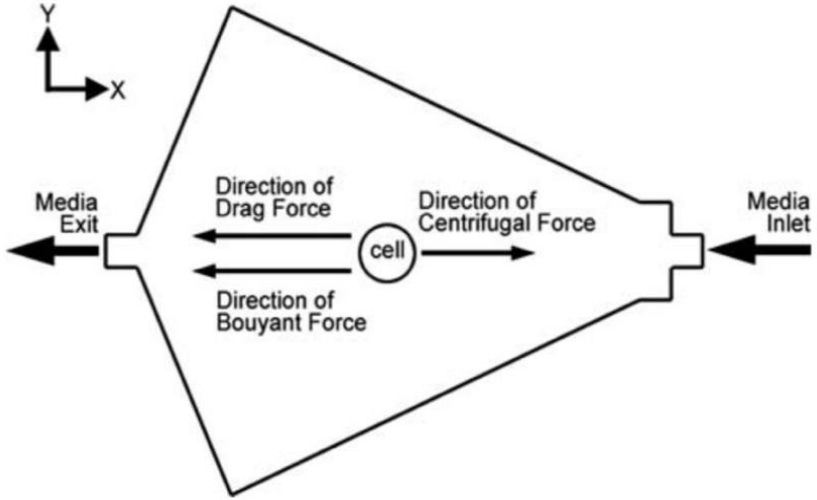
BAD: inefficient/expensive, cells can get exhausted, **patient specific** – small scale, data vulnerability

Van Wie Lab: Bioreactor for Immunotherapy



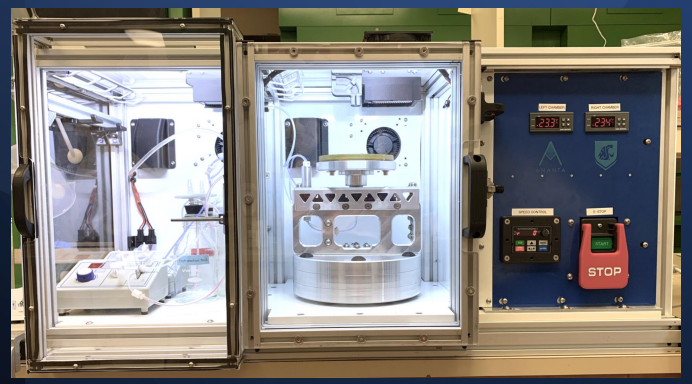
Centrifugal Bioreactor (CBR)

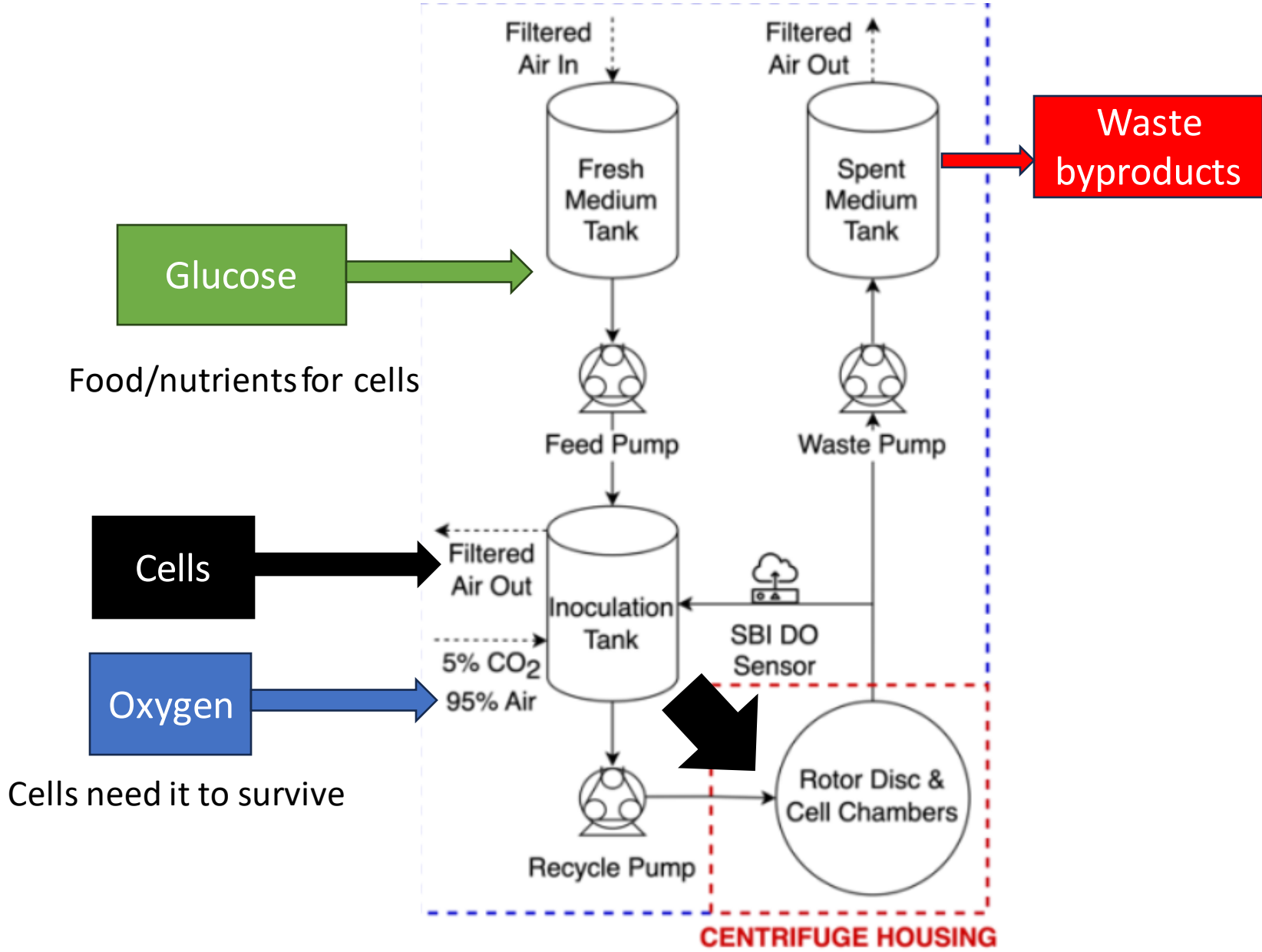




- Application: growth of T cells for cancer immunotherapy

Bioreactor Process Flow





Mathematical Modeling of CBR

$$\frac{\partial C_{cell}}{\partial t} = \mu_{max} \cdot \left(1 - \frac{C_L}{C_{L\_max}}\right)^n \cdot \left(1 - \frac{C_A}{C_{A\_max}}\right)^m \cdot C_{Cell}$$

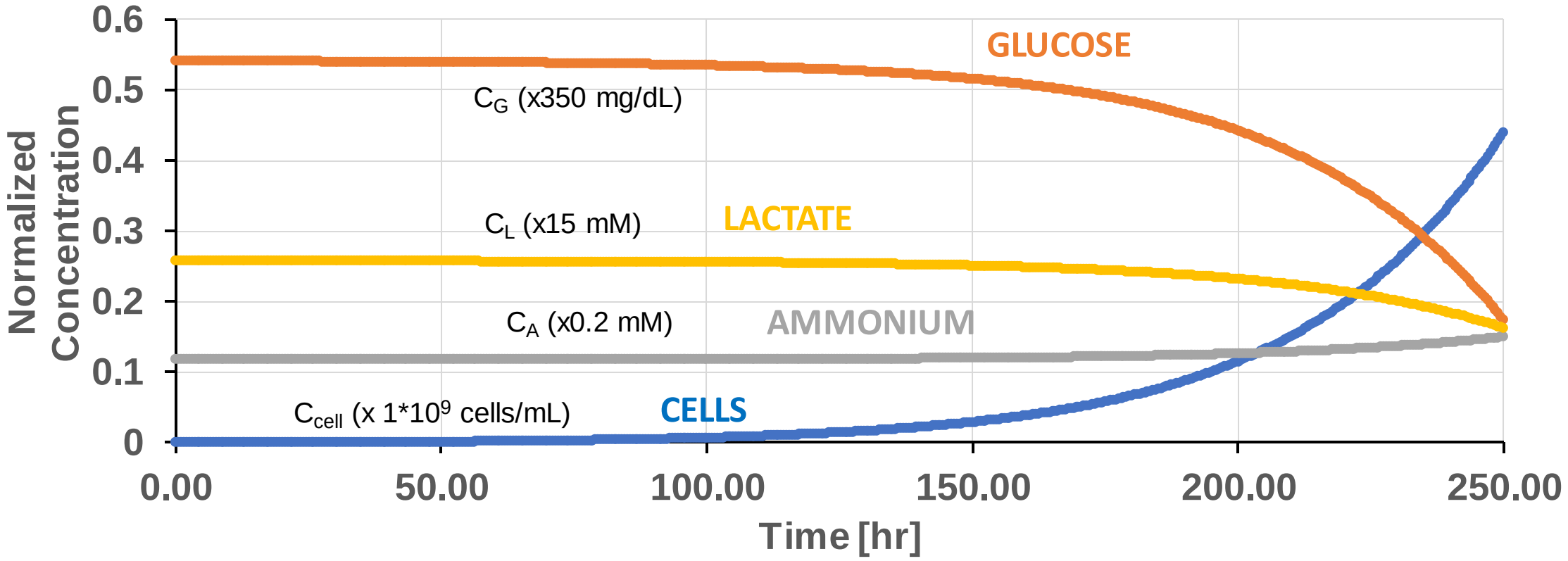
$$\frac{\partial C_G}{\partial t} = D(C_{G0} - C_G) - Y_{GC} \cdot \left(\frac{\partial C_{Cell}}{\partial t}\right)$$

$$\frac{\partial C_A}{\partial t} = D(C_{A0} - C_A) + Y_{AC} \cdot \left(\frac{\partial C_{Cell}}{\partial t}\right)$$

$$\frac{\partial C_L}{\partial t} = D(C_{L0} - C_L) + Y_{LC} \cdot \left(\frac{\partial C_{Cell}}{\partial t}\right)$$

- C_{cell} = cell density
- Glucose (G)
- Ammonium (A)
- Lactate (L)

Model Predictions



Bioreactor Development and Progress

- Completed work:
  - Optimized cell growth, built reactor – **More cells in less time vs. industry standard**
    - Kaiphanliam et al, 2023, *Biotech Progress*
- Automation: testing sensors
  - Sensors read O2 data in real-time
  - Script -> sends data from online sensor software to Excel, compares to model prediction

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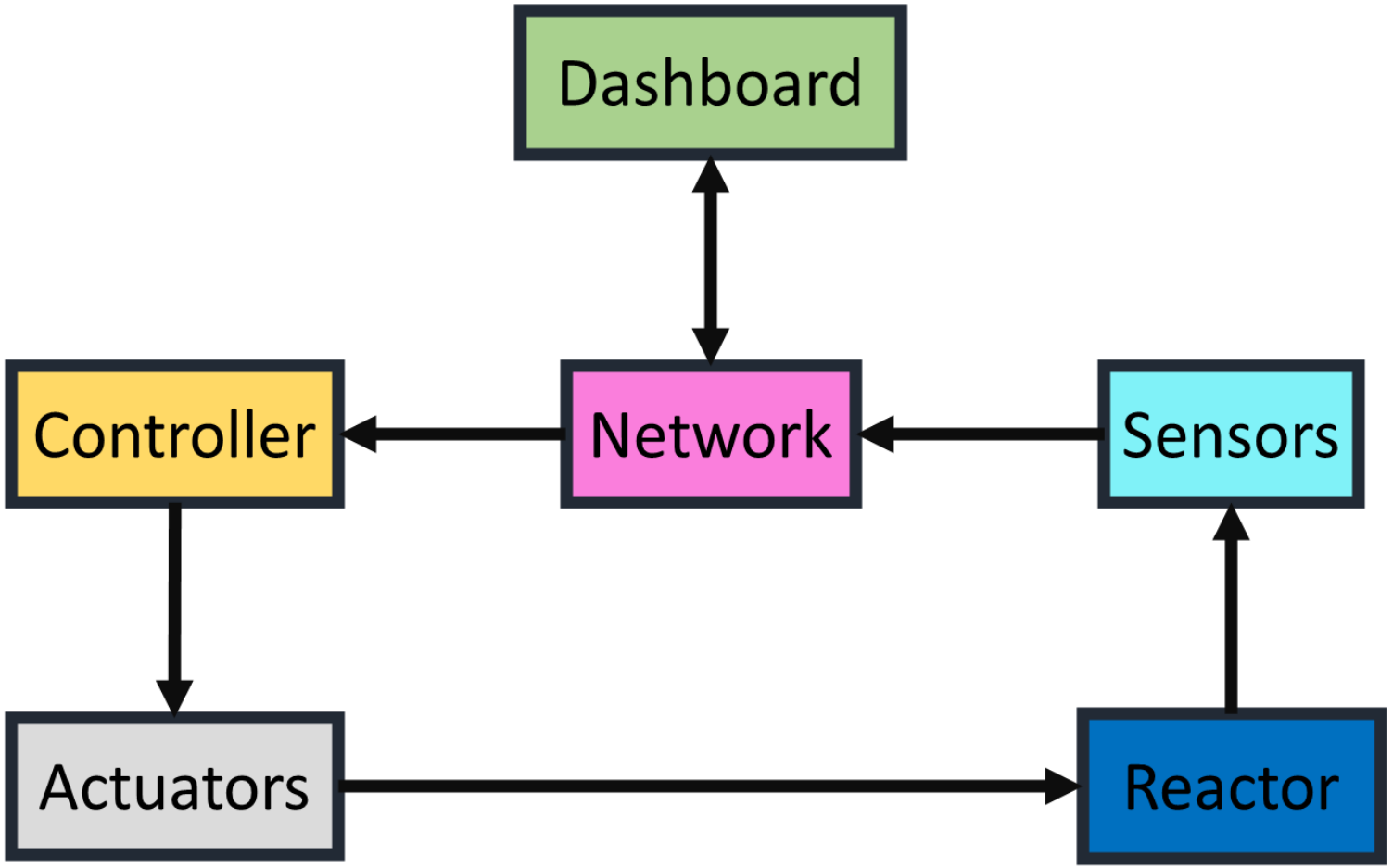
DOTS a platform by sbi

WPI WORLD PRECISION INSTRUMENTS

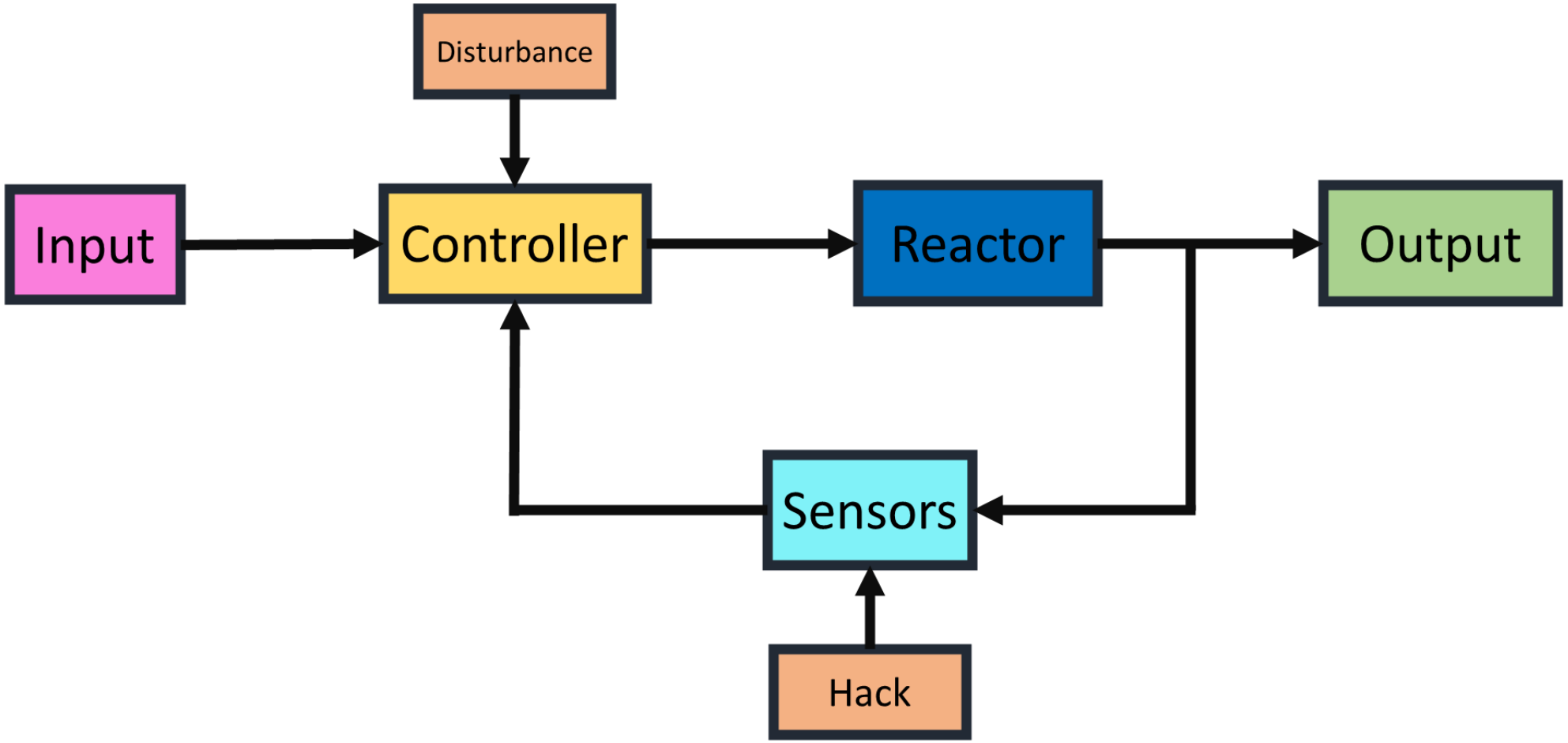
Next Steps and Future Work

- **How can we automate our process and predict the impact of cyberattacks?**
- Prevent cell dysfunction in real time
  - Online/remote access
  - Sensors: detect **glucose/oxygen**
  - Feedback control -> adjust feed rates
- Simulations: determine how hacks introduce false data that breaks automation – **Matlab/Simulink**

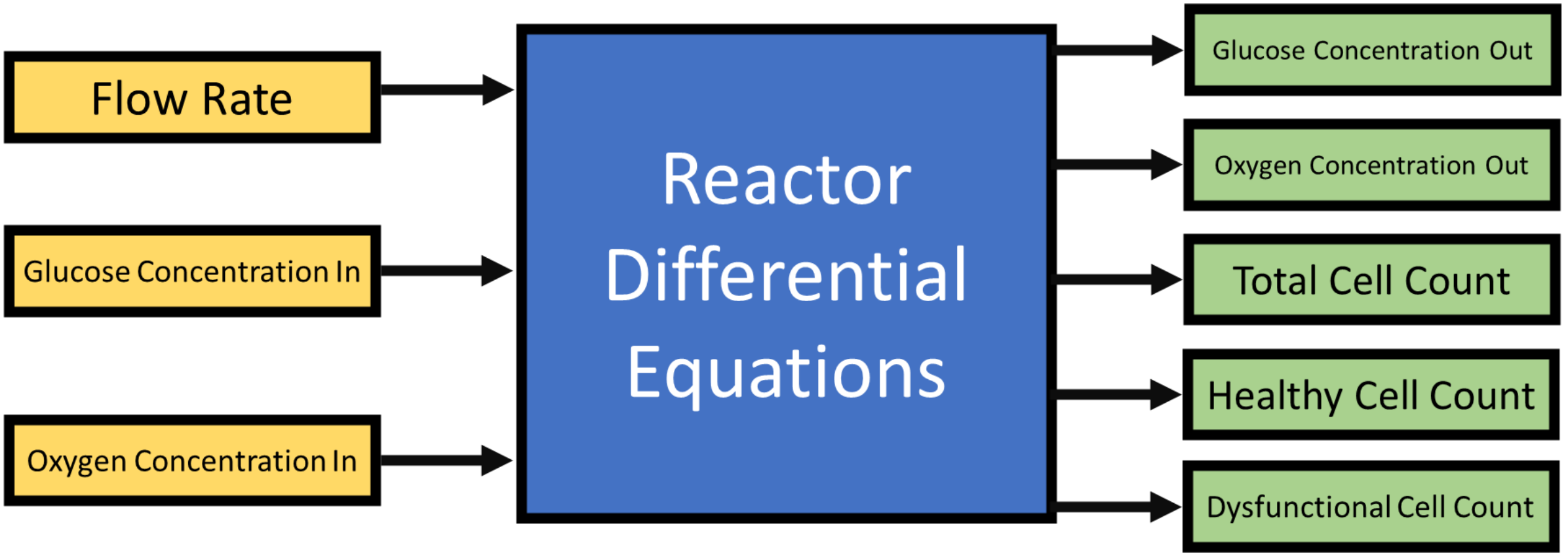
Automation of Bioreactor Process



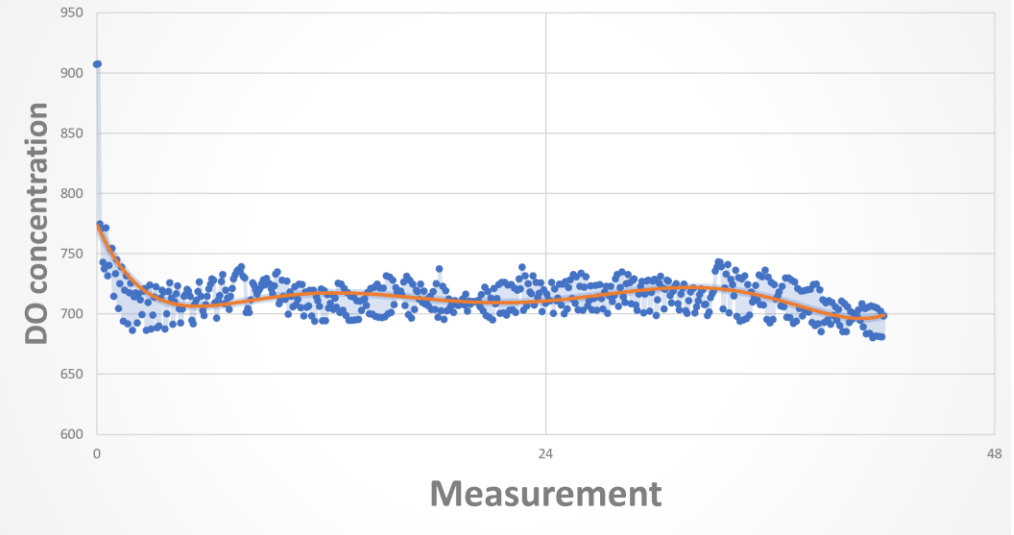
MATLAB Simulink Model Outline

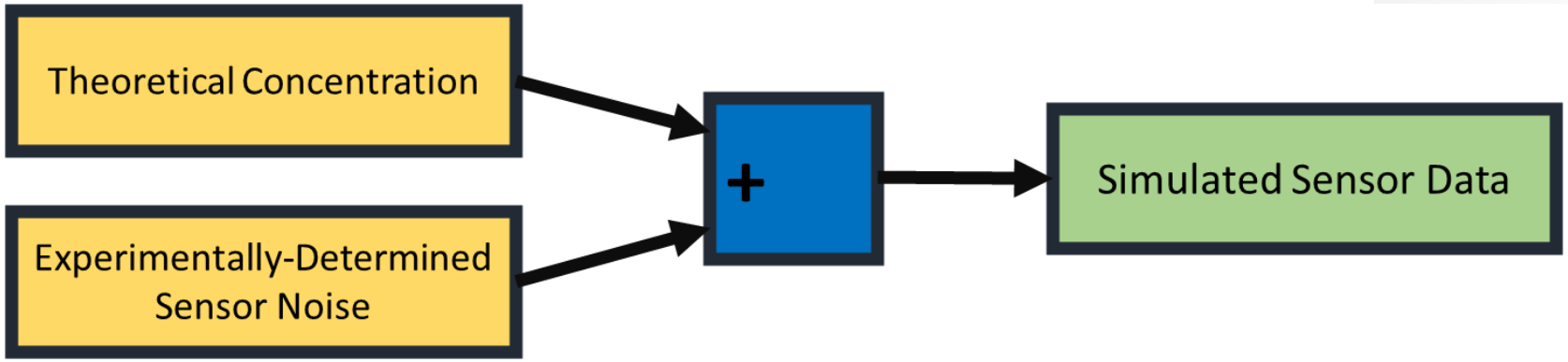


Reactor Model

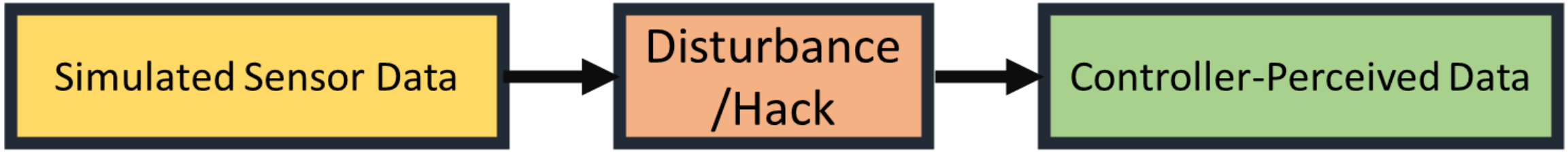


Sensor Model



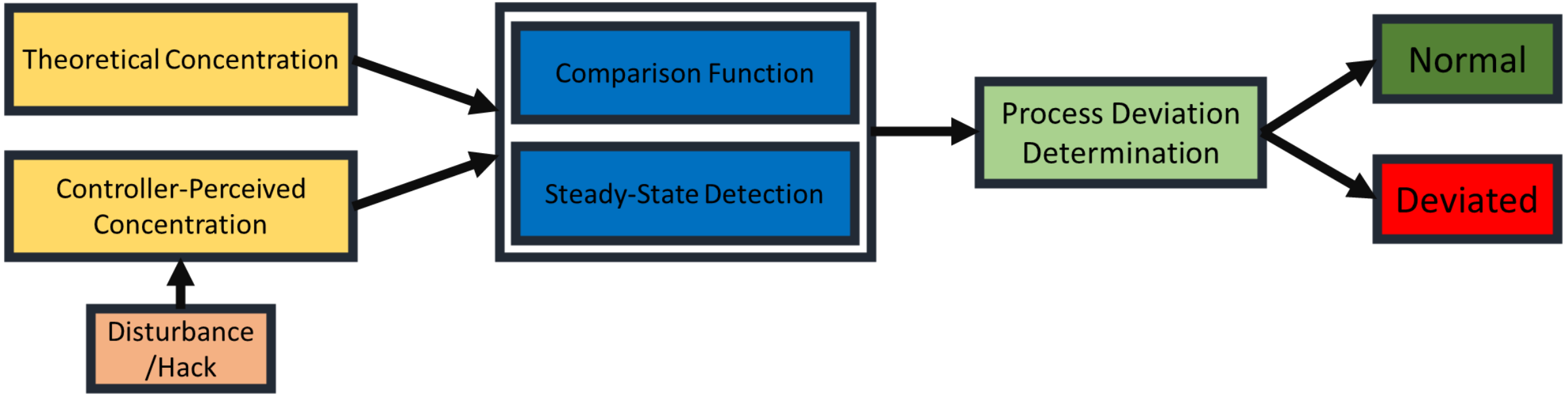


Disturbance and Hack Model

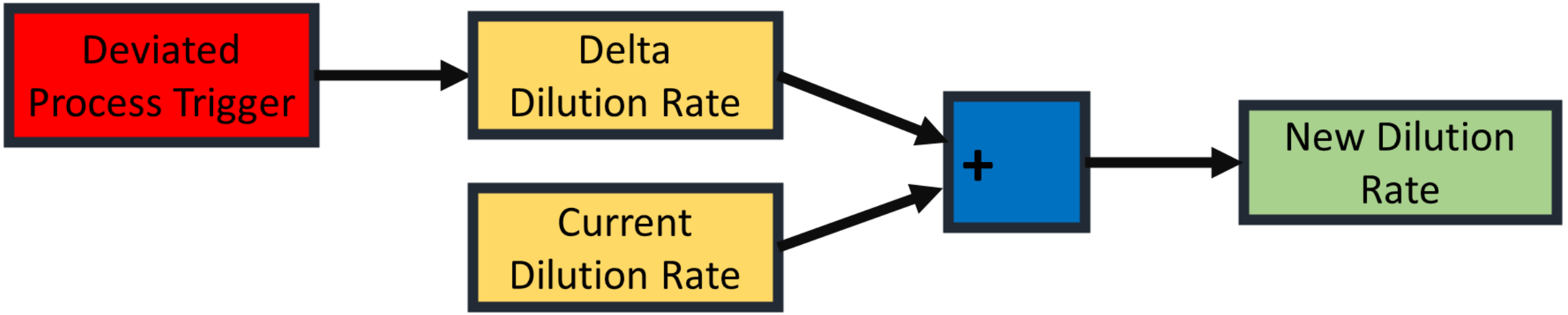


$$Hacked\ Sensor\ Value = (Actual\ Sensor\ Value) * Scaling\ Factor + Fixed\ Value$$

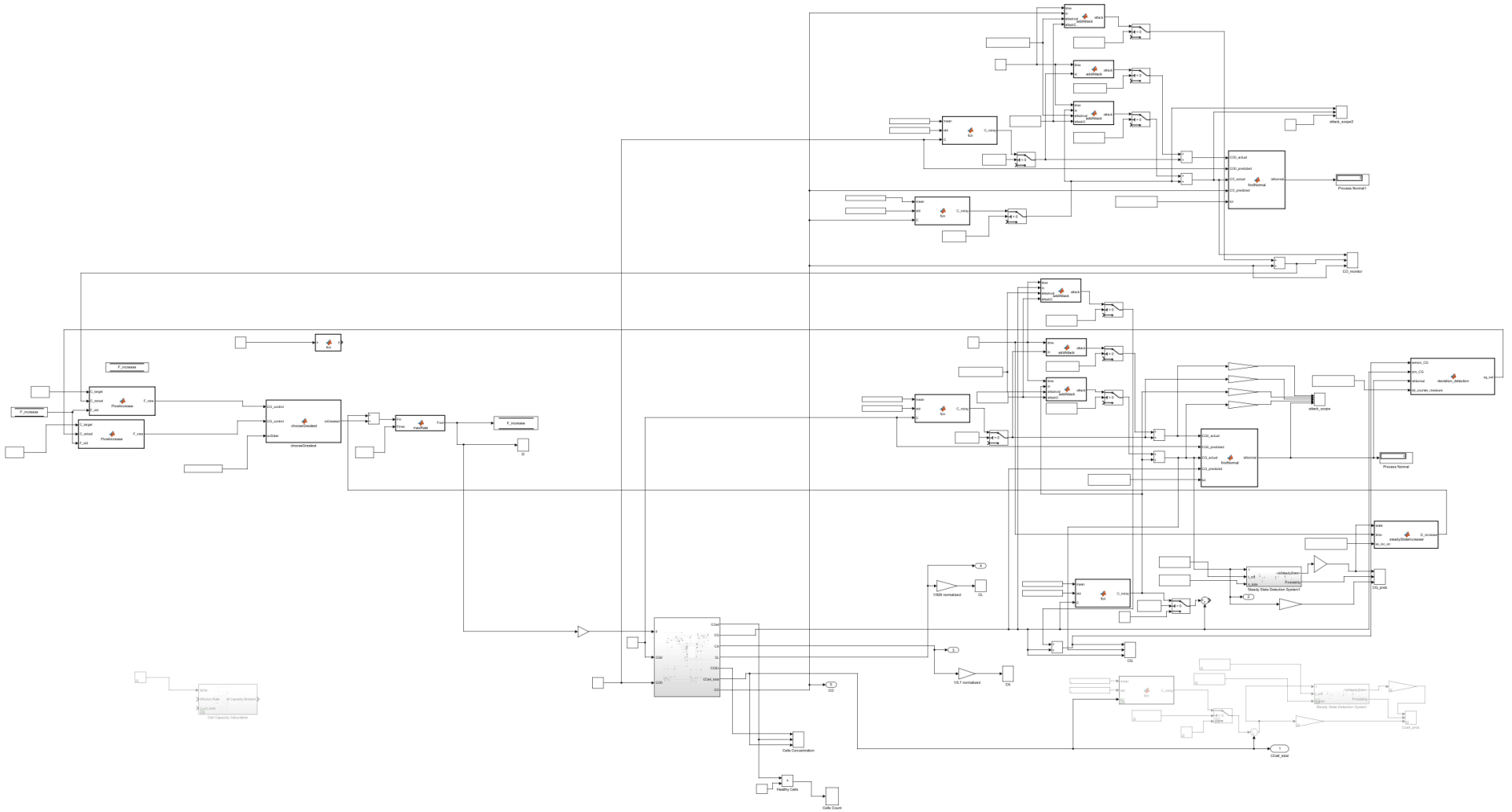
Disturbance Detection Model



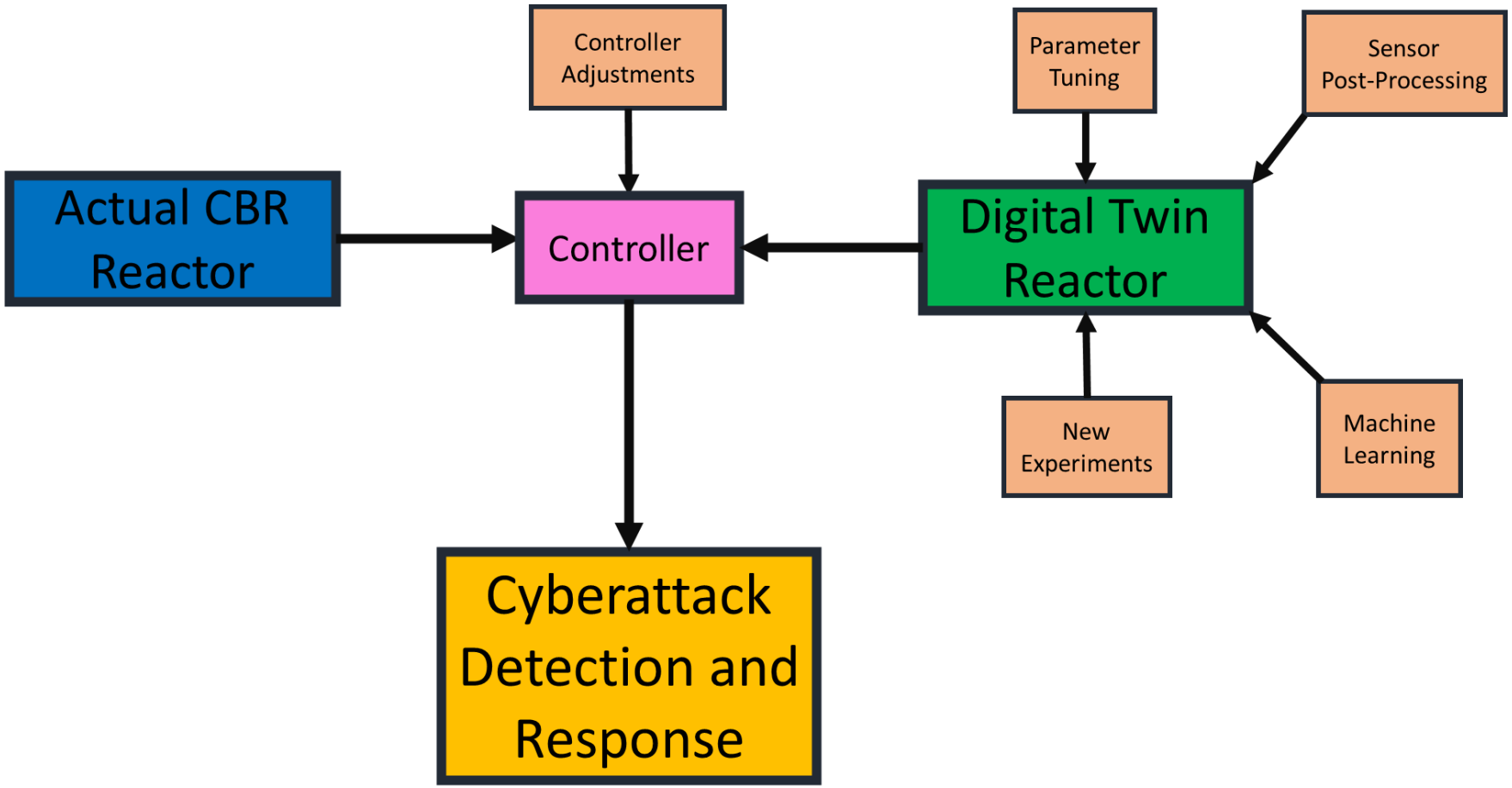
Disturbance Response Model



Simulink!



Future Plan: Feedback Control



Thank you! Questions?

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Cougar Cage

National Institutes of Health

GRIFFISS INSTITUTE

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Sources

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