University of Idaho
College of Science

CARNEGIE R1 CLASSIFIED UNIVERSITY

Systems Medicine
of Infectious Diseases
Research and Consulting Group

Adaptive Observers for Medical Digital Twins

A Framework for personalized medicine

Juan E. Sereno
Department of Mathematics and Statistical Science
University of Idaho

Panel 1. A 52-year-old male with a history of stroke and hemiplegia is found confused in his prison cell.

Taken, and adapted with Gemini, from:

[1] Laubenbacher, R., Mehrad, B., Shmulevich, I., & Trayanova, N. (2024). **Digital twins in medicine**. Nature Computational Science, 4(3), 184-191.

Panel 1. A 52-year-old male with a history of stroke and hemiplegia is found confused in his prison cell.

Panel 2. At ED, patient presents hypotension, mild renal insufficiency, and bilateral airspace disease on chest X-ray.

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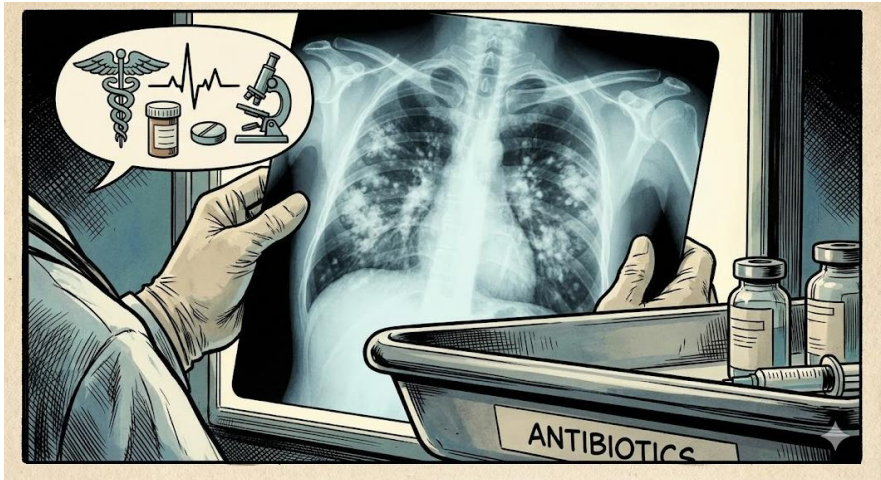

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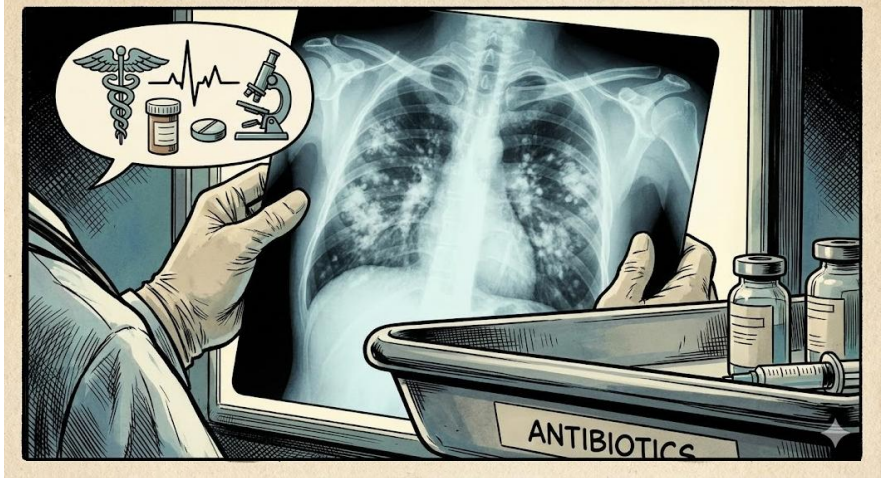
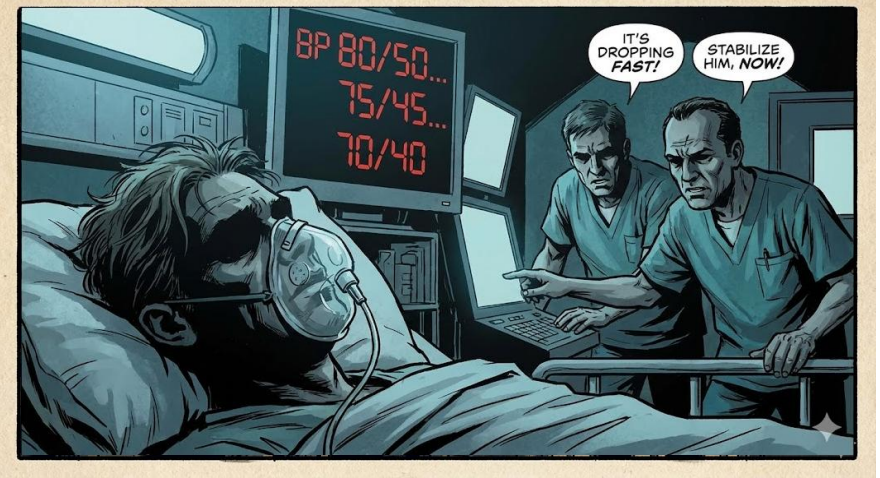


Panel 4. 6 h later, recurrent hypotension requiring intravenous pressors and escalating supplemental oxygen.



Suspected pathogen: **Klebsiella pneumoniae**.

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Panel 5. 3 h after deterioration, requires endotracheal intubation and mechanical ventilation for ARDS-induced hypoxic respiratory failure.

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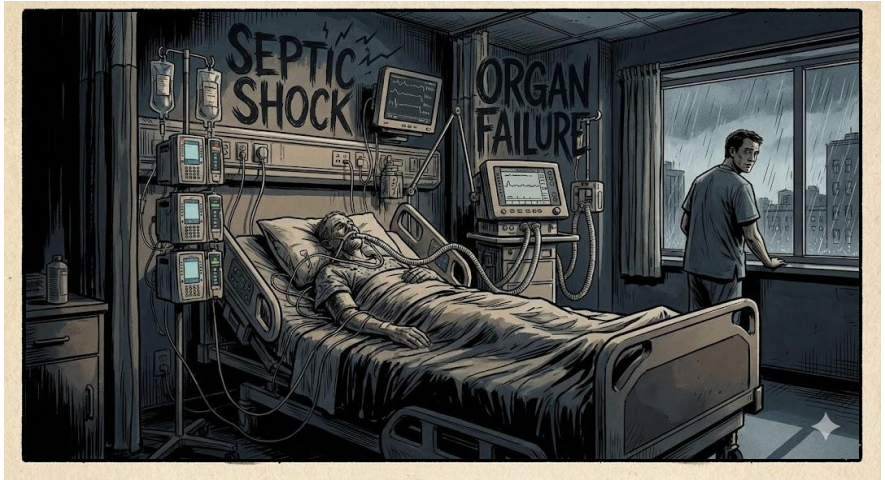
Panel 6. Condition progress to refractory septic shock and acute kidney injury ***despite receiving antibiotics to which the Klebsiella pneumoniae was sensitive***.



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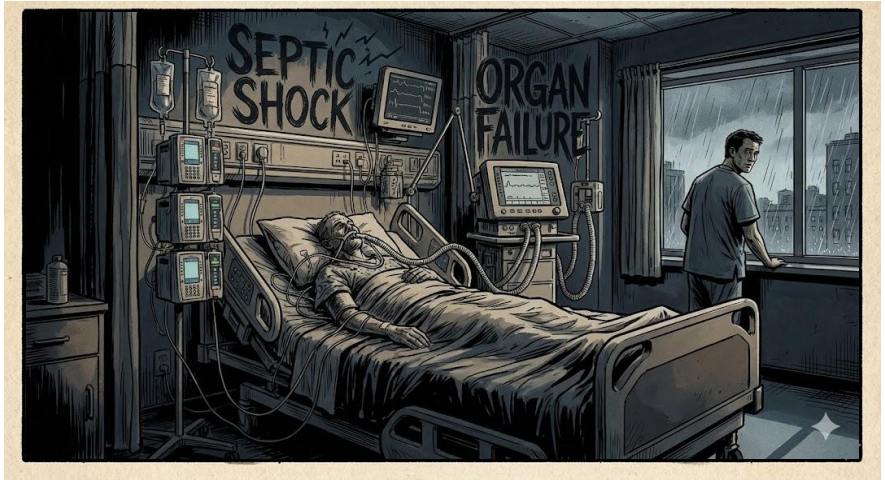

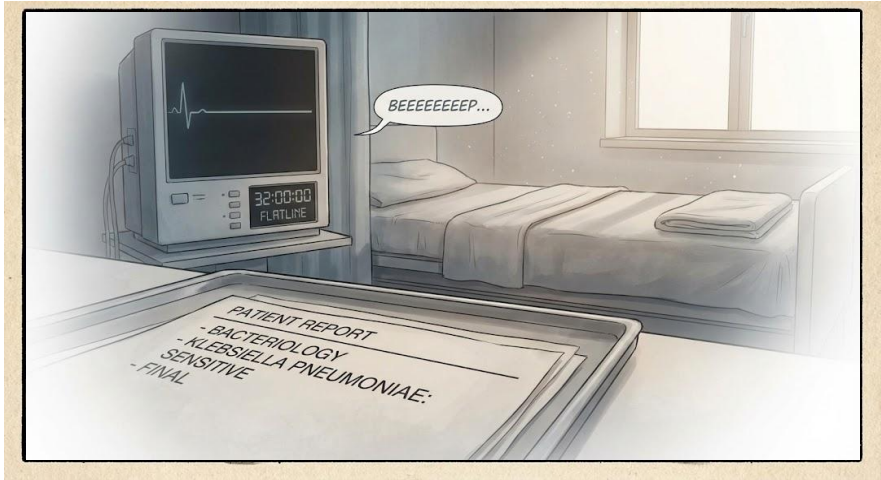

Panel 7. Patient dies of multi-organ failure 32 hours after presentation.

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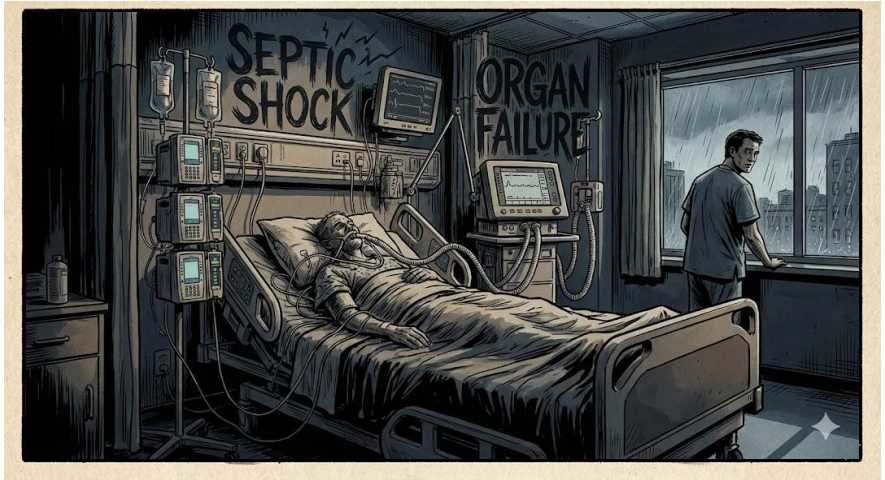

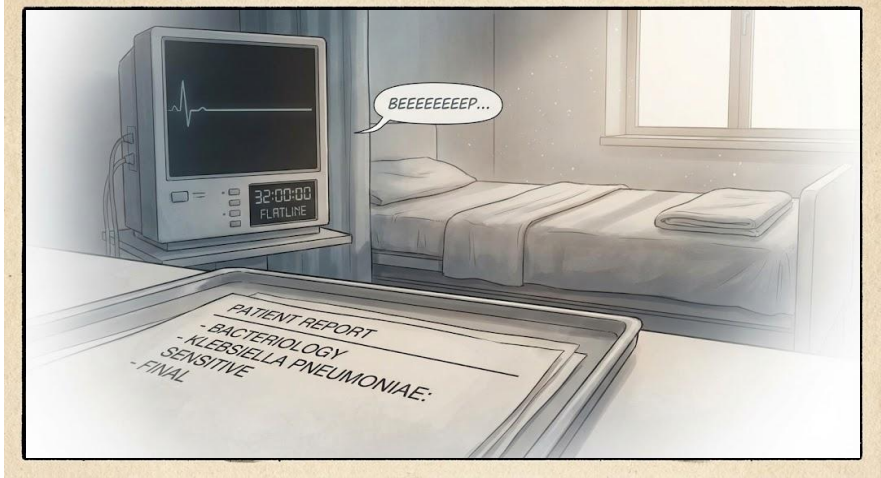

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Why we need Digital Twins in medicine?
This one represent the biggest promise and challenge in applying computational modeling at the level of individual patients, i.e., personalized medicine.

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What is a Digital Twin in Medicine?

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***Digital Twin* [2]:**

1. A model of the physical twin.
2. An evolving set of data relating to the object, and
3. A means of dynamically updating or adjusting the model in accordance with data.

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NASA reports [3]:
A ***digital twin*** is an integrated multiphysics, muti-scale, probabilistic simulation of a vehicle or system that uses the best available physical models, sensor updates, feet history, etc., to mirror the life of its flying twin. The ***digital twin*** is ultra-realistic and may consider one or more important and interdependent vehicle systems, including propulsion and energy Storage, life support, avionics, thermal protection, etc.

Taken from: **[3]** Shafto, M., M. Conroy, R. Doyle, E. Glaessgen, C. Kemp, J. LeMoigne, and L. Wang. 2012. "***Modeling, Simulation, Information Technology and Processing Roadmap.***" National Aeronautics and Space Administration 32(2012):1–38.

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A trade-off arise

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Medical Digital Twin **[1,4]:**

A computational model of the system to be twinned (heathy or sickness processes) that is connected to the physical twin in a bidirectional fashion over time, periodically recalibrated with patient data, and provides patient predictions over time to prevent or treat diseases.

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[1] Laubenbacher, R., Mehrad, B., Shmulevich, I., & Trayanova, N. (2024). **Digital twins in medicine**. Nature Computational Science, 4(3), 184-191.
[4] ***Foundational Research Gaps and Future Directions for Digital Twins*** (National Academies of Sciences, Engineering and Medicine, 2023); https://doi.org/10.17226/26894.

Digital Twins in Medicine

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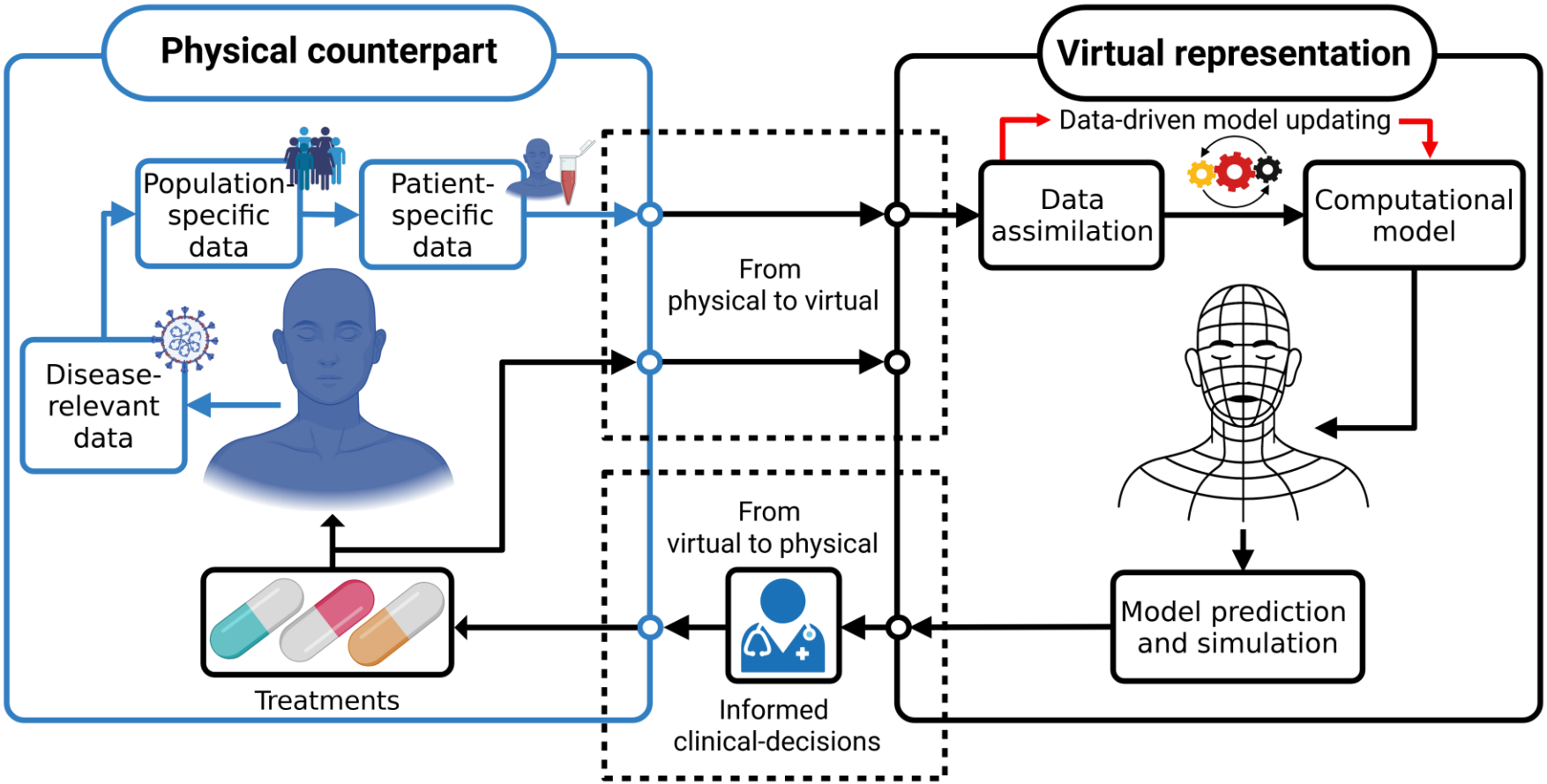

Figure 1.a. The standard Digital Twin Framework **[5]** .

Taken from:

[5] Sereno, J. E., Neujahr, H., Hernandez-Gonzalez, M., & Hernandez-Vargas, E. A. (2025). ***Iterative calibration of medical digital twins via adaptive estimators***. Frontiers in Applied Mathematics and Statistics, 11, 1699390.

Digital Twins in Medicine

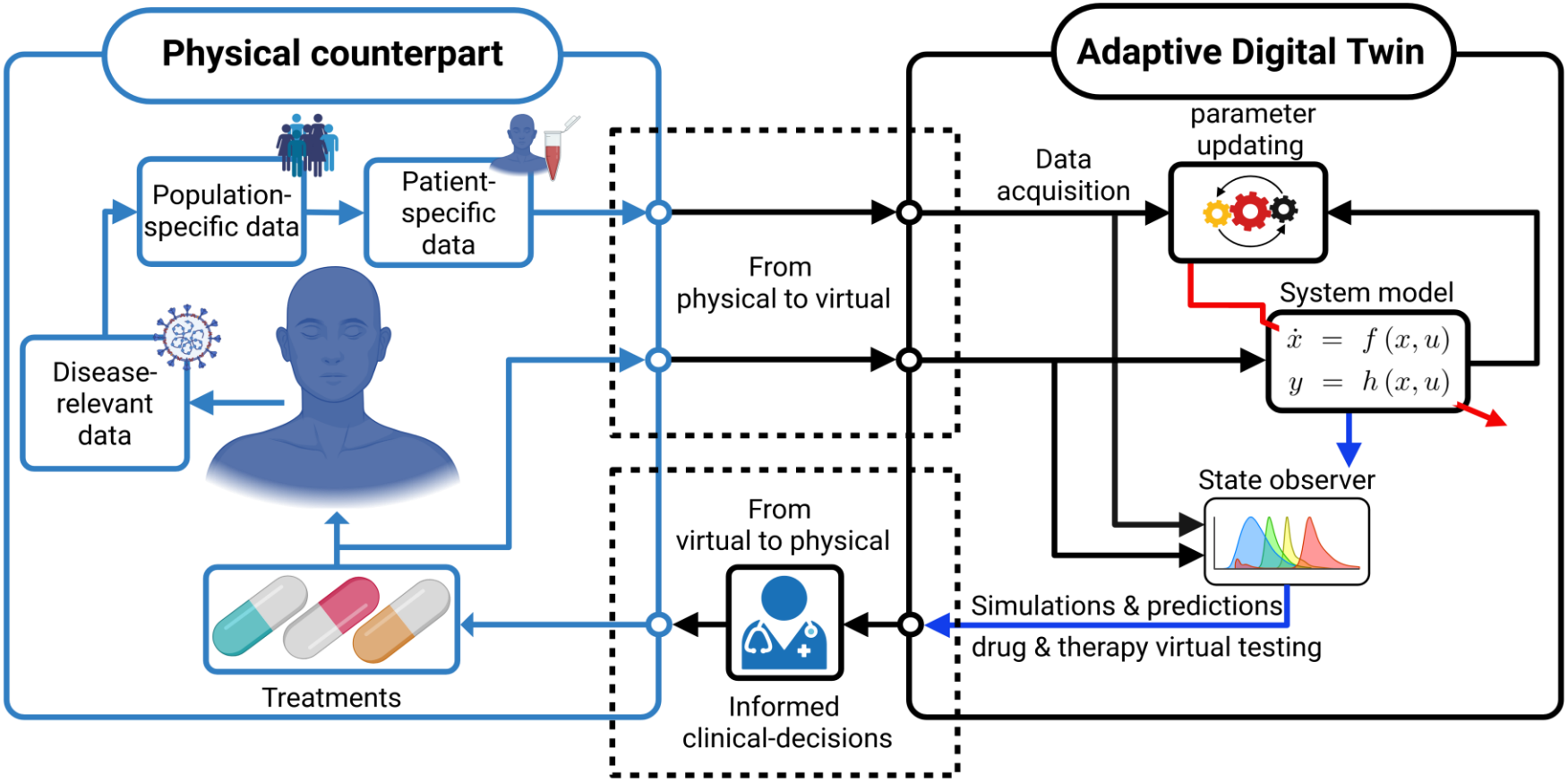

Figure 1.b. Adaptive Digital Twin Framework **[5]** .

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Mathematical foundations for model parameter updating

Model Parameter Updating:

1. Adaptive Observers **[6]**.
2. Hybrid Extended Kalman Filter **[7]**.

Taken from:

[6] Besancon, G., de León-Morales, J., & Huerta-Guevara, O. (2006). ***On adaptive observers for state affine systems***. International journal of Control, 79(06), 581-591.

[7] Simon, D. (2006). ***Optimal state estimation: Kalman, H infinity, and nonlinear approaches***. John Wiley & Sons.

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Biomedical applications:

1. HIV mutation model **[8]**.
2. Antimicrobial Resistance model **[9]** .

Taken from:
[8] Hernandez-Vargas, E. A., & Middleton, R. H. (2013). ***Modeling the three stages in HIV infection***. Journal of theoretical biology, 320, 33-40.
[9] Hernández-Vargas, E. A., Parra-Rojas, C., & Olaru, S. (2021, December). ***Switching logistic maps to design cycling approaches against antimicrobial resistance***. In 2021 60th IEEE conference on decision and control (CDC) (pp. 4248-4253). IEEE.

HIV mutation model

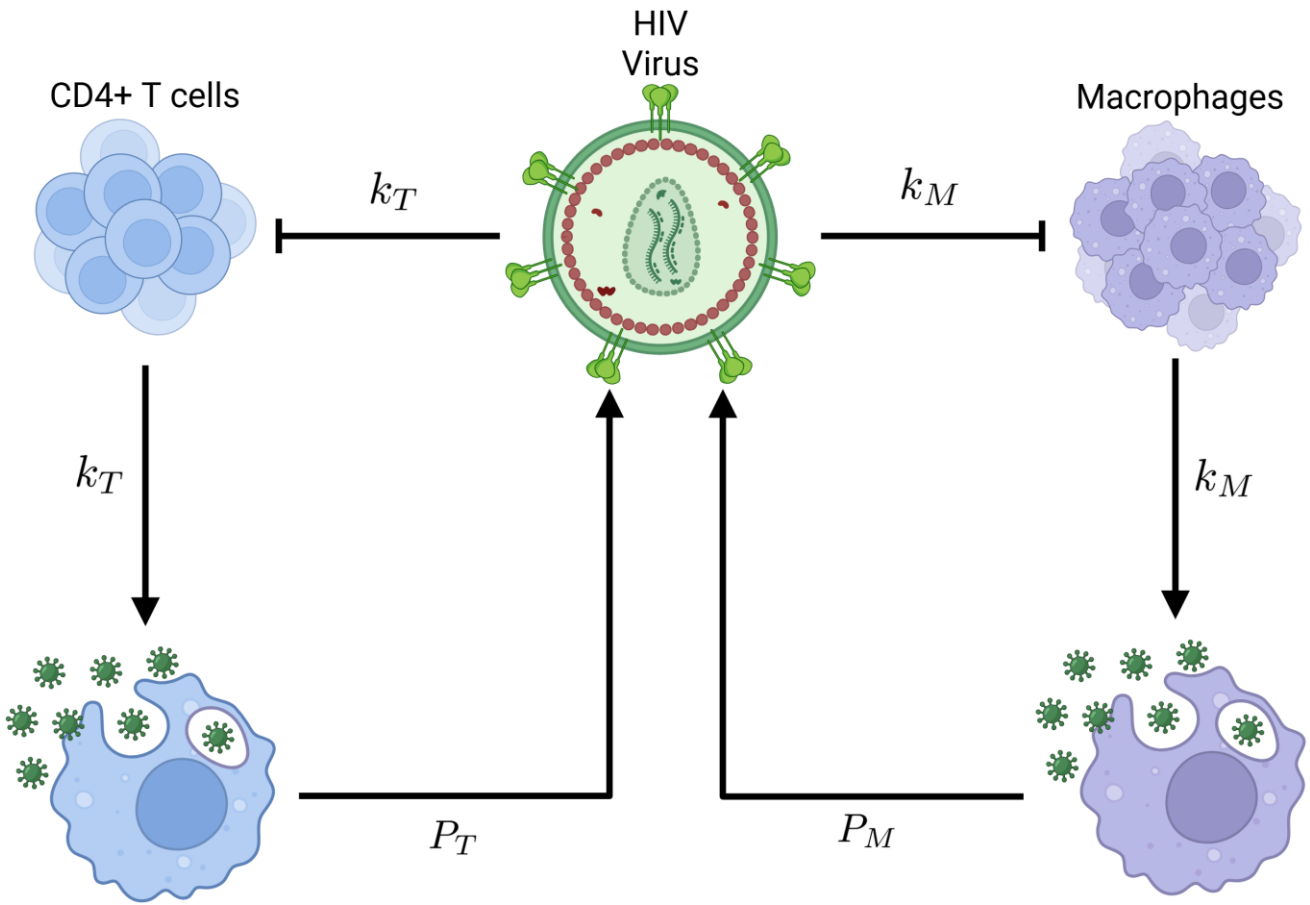

Figure 2. HIV infection scheme, taken from **[8]**.

Taken from:
[8] Hernandez-Vargas, E. A., & Middleton, R. H. (2013). **Modeling the three stages in HIV infection**. Journal of theoretical biology, 320, 33-40.

HIV mutation model

$$\dot{T} = s_T + \frac{\rho_T}{C_T + V_T} T V_T - \sum_{i=1}^{n} k^i_{T,\sigma} T V_i - \delta_T T$$

$$\dot{M} = s_M + \frac{\rho_M}{C_M + V_T} M V_T - \sum_{i=1}^{n} k^i_{M,\sigma} M V_i - \delta_M M$$

$$\dot{T}^*_i = k^i_{T,\sigma} T V_i + \sum_{j=1}^{n} \mu m_{i,j} V_j T - \delta_{T^*} T^*_i$$

$$\dot{M}^*_i = k^i_{M,\sigma} M V_i + \sum_{j=1}^{n} \mu m_{i,j} V_j M - \delta_{M^*} M^*_i$$

$$\dot{V}_i = p^i_{T,\sigma} T^*_i + p^i_{M,\sigma} M^*_i - \delta_V V_i .$$

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$$\dot{V}_i = p^i_{T,\sigma} T^*_i + p^i_{M,\sigma} M^*_i - \delta_V V_i . \qquad (1)$$

Can we update model parameters to estimate infections rates and the number of infected cells from measurements?

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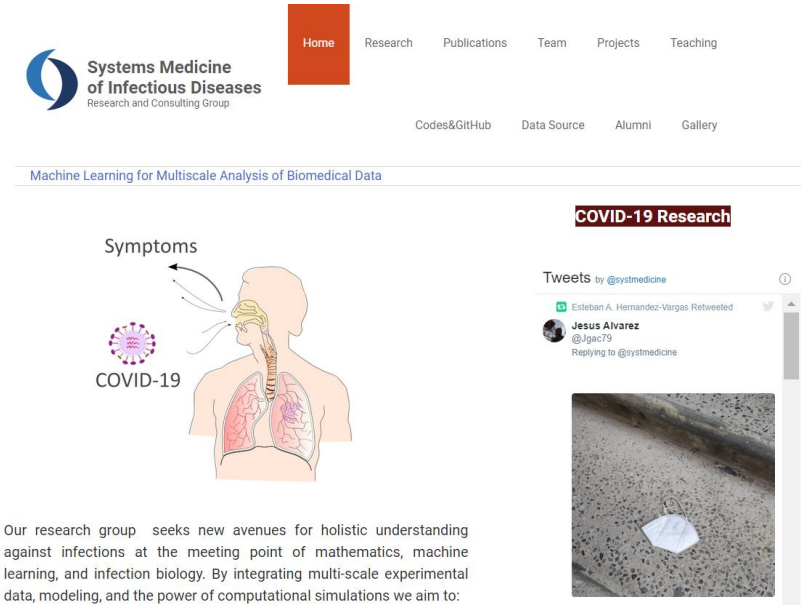

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References

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[3] Rodríguez, A., et al. An adaptive observer for operation monitoring of anaerobic digestion wastewater treatment. J. Chem. Eng. 269 (2015): 186-193.

[4] Hernandez-Vargas, E. A. (2019). Modeling and control of infectious diseases in the host: with MATLAB and R. Academic Press.