Personalizing agent-based models to construct medical digital twins

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Outline and Land Acknowledgement

- Data Assimilation (DA) Background
  - Kalman Filters (KFs)
- Stochastic, Multiscale Models
  - Agent-Based Models (ABMs)
  - Micro-states and Macro-states
- Results: DA on ABMs
  - Example: Viral Infection ABM
  - Micro-state Synthesis and Quantization
- **Land acknowledgement:** Mascogo, Miccosukee, Nacotchtank (Anacostan), Piscataway, Seminole, and Timucua (Nations, Tribes, and People)

A.C. Knapp, D.A. Cruz, B. Mehrad, and R.C. Laubenbacher. *Journal of the Royal Society Interface* **22** (2025): 20250055

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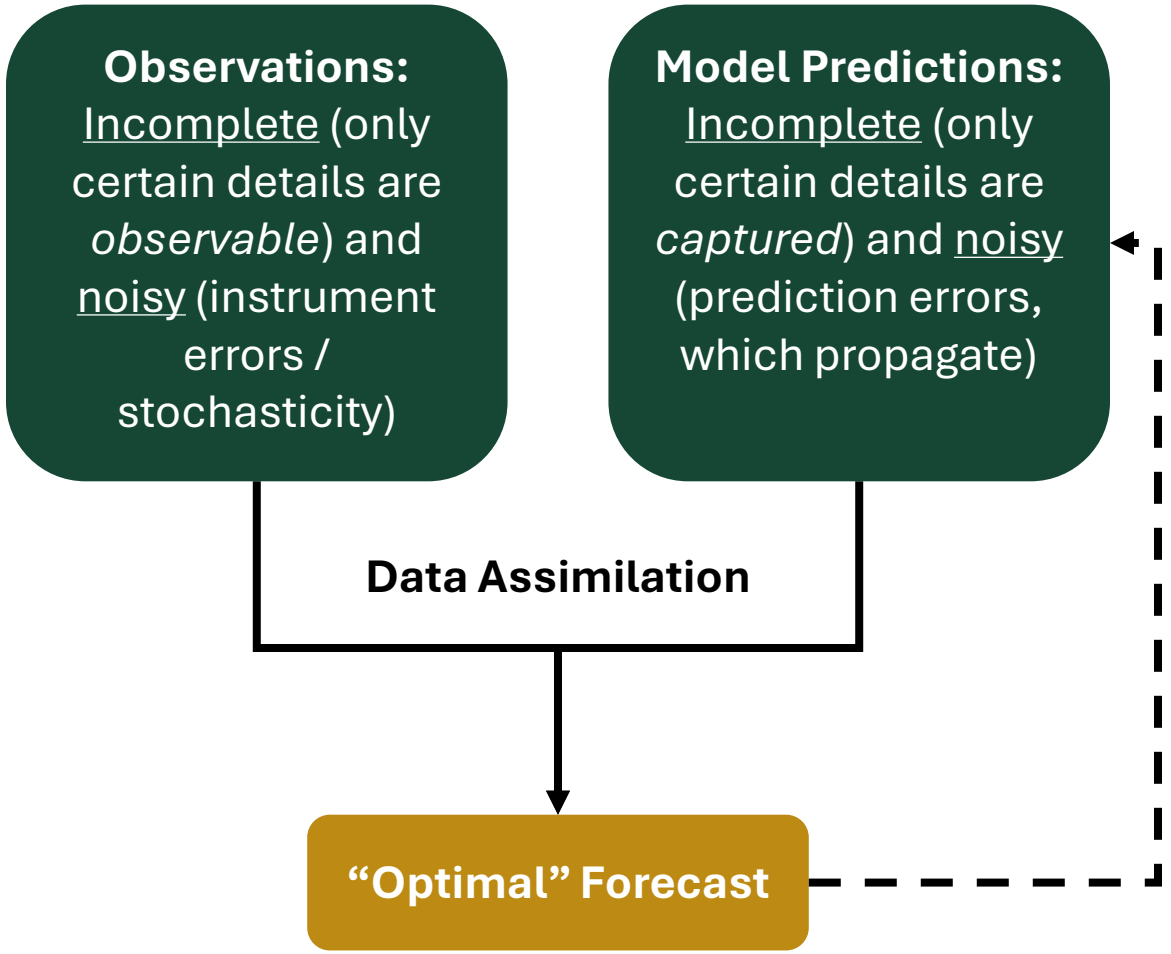
Data Assimilation (DA) Overview

- **Idea:** Given model predictions and observations, DA seeks to produce an "optimal" estimate of current and future states of a target system
- Brief History
  - Numerical Weather Prediction
  - Different implementations: initial condition estimation, model parameterization / personalization, interpolation, **single vs repetitive**, etc.



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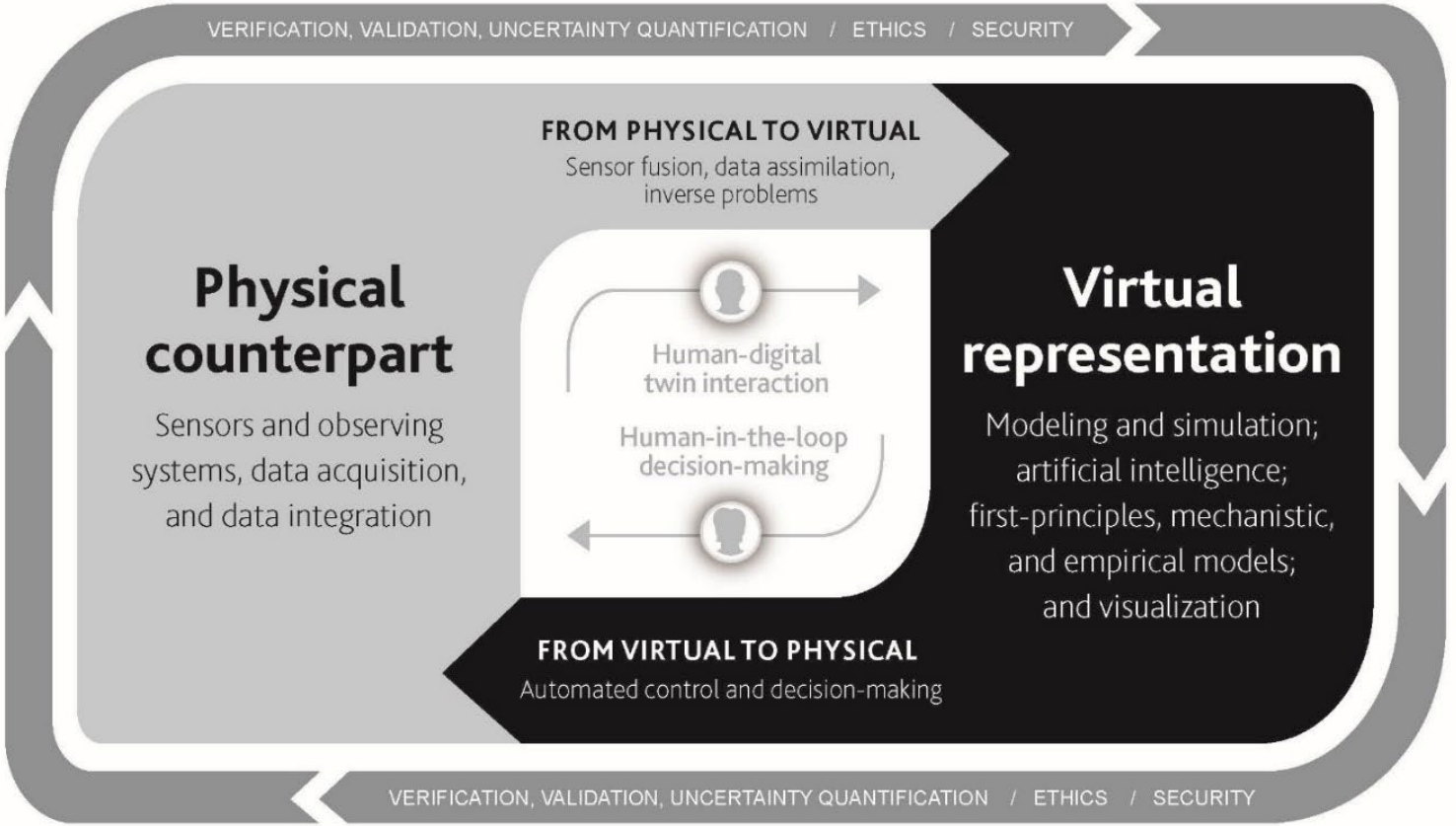
Medical Models and Digital Twins

- Medical Digital Twins: An “up-to-date” model which changes with patient and informs medical decisions



National Academies of Sciences, Engineering, and Medicine. 2023. *Foundational Research Gaps and Future Directions for Digital Twins*. https://doi.org/10.17226/26894

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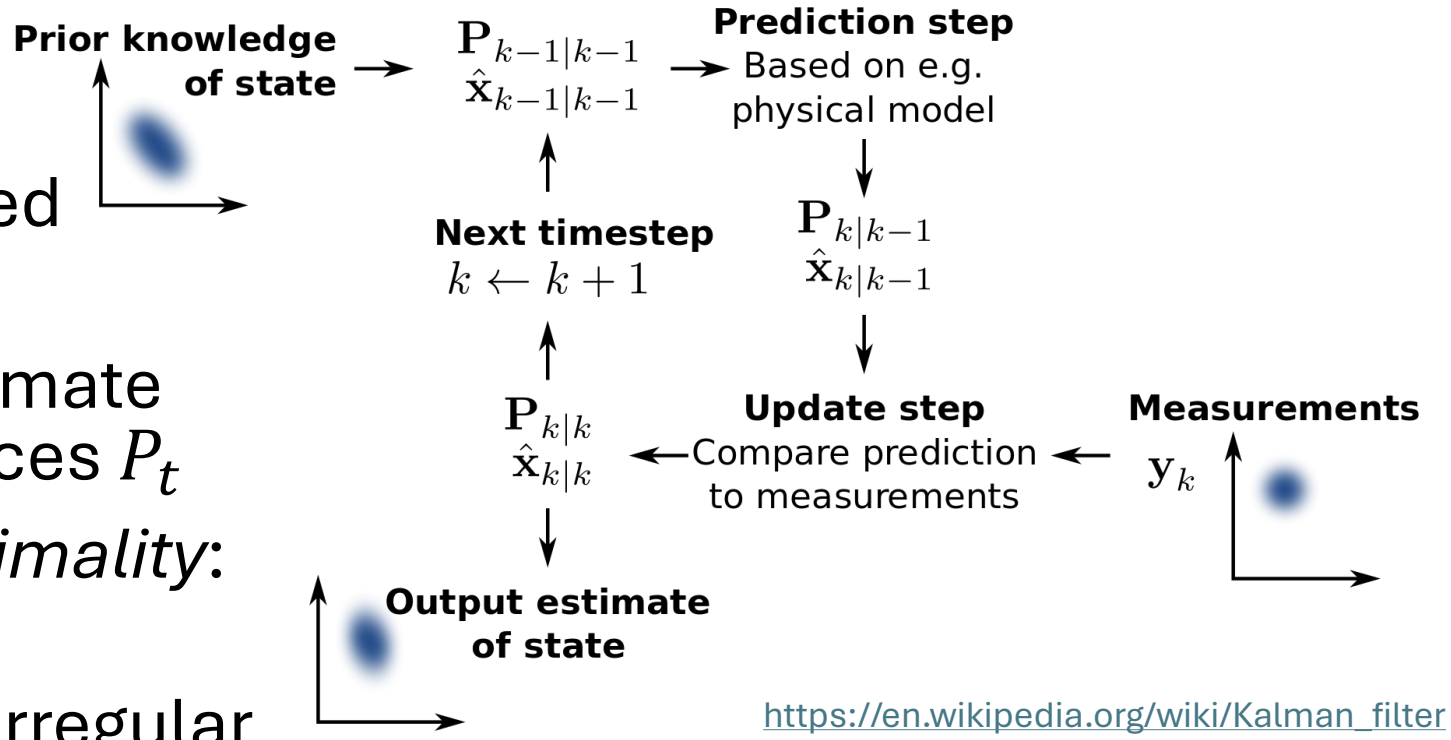
The Kalman Filter (KF)

- *Optimal* algorithm; minimizes mean squared error of estimates
- Predict and update estimate means $\hat{x}_t$ and covariances P_t
- *Key assumption for optimality*: All noise is Gaussian
- Measurements can be irregular
- Traditionally used for ODE/PDE models
- KF Variants: Unscented KF (UKF), **Ensemble KF (EnKF)**, etc.



https://en.wikipedia.org/wiki/Kalman_filter

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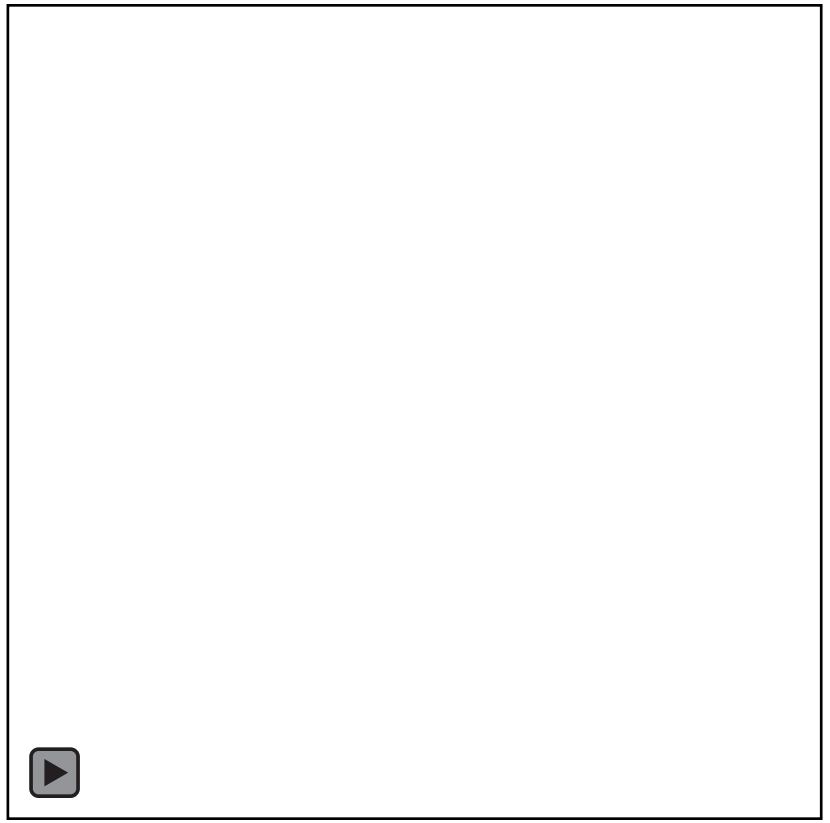
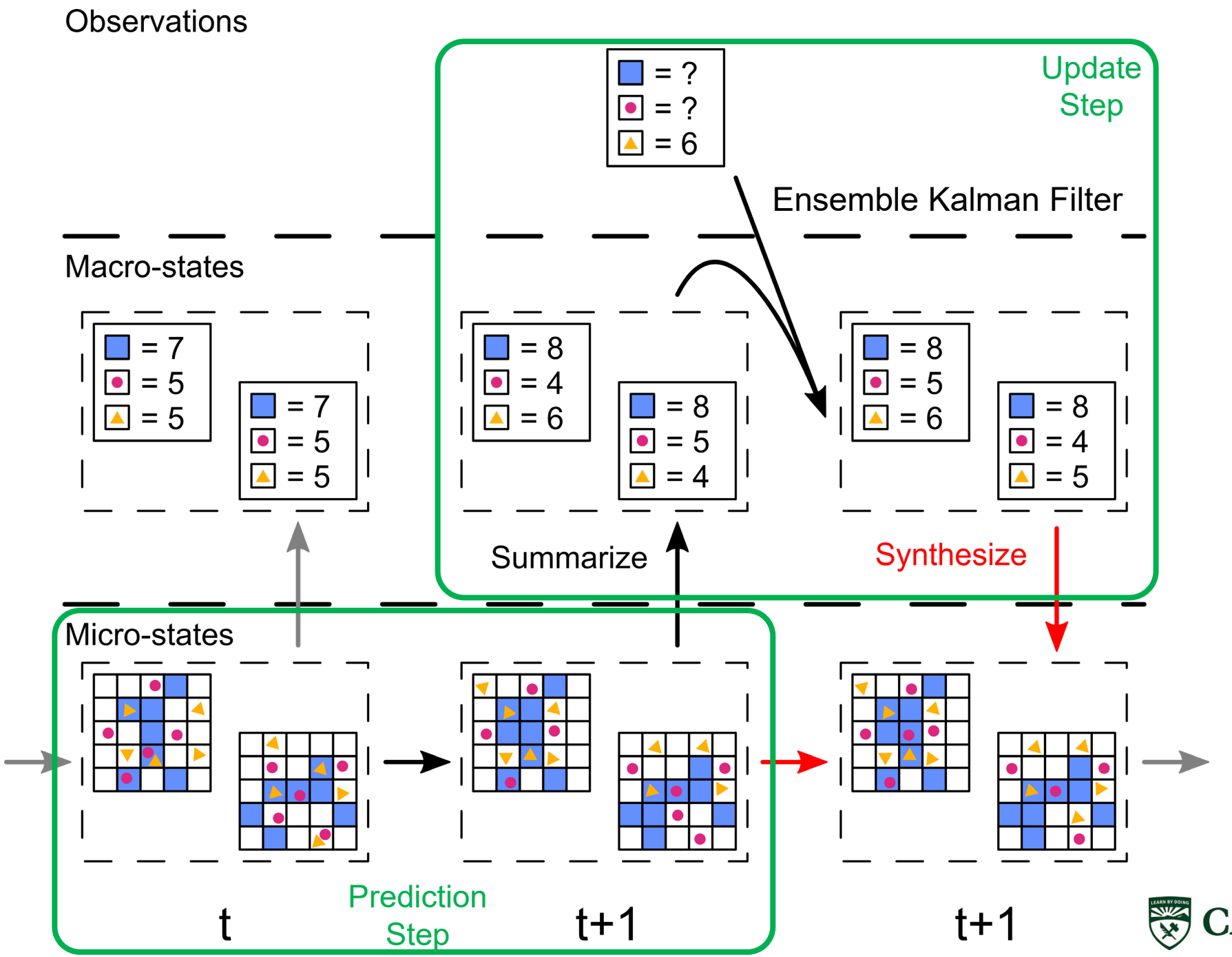
Applying KF to Stochastic, Multiscale Models

- Agent-based models (ABMs)
  - **ABM:** Computational model for simulating autonomous agents which captures how local interactions affect the system overall
  - ABMs are typically stochastic and/or multiscale, with a highly variable state space
  - **Micro-state space:** Complete description of variable / attribute values for each agent at time t; model may several parameters
  - **Macro-state space:** Summarized description of aggregate variables across all agents at time t (e.g., agent counts)



Cockrell and An 2021. Viruses.
Reimplementation and simulation by A. Knapp.

ABMKF – Updating ABM Macro-states* via DA



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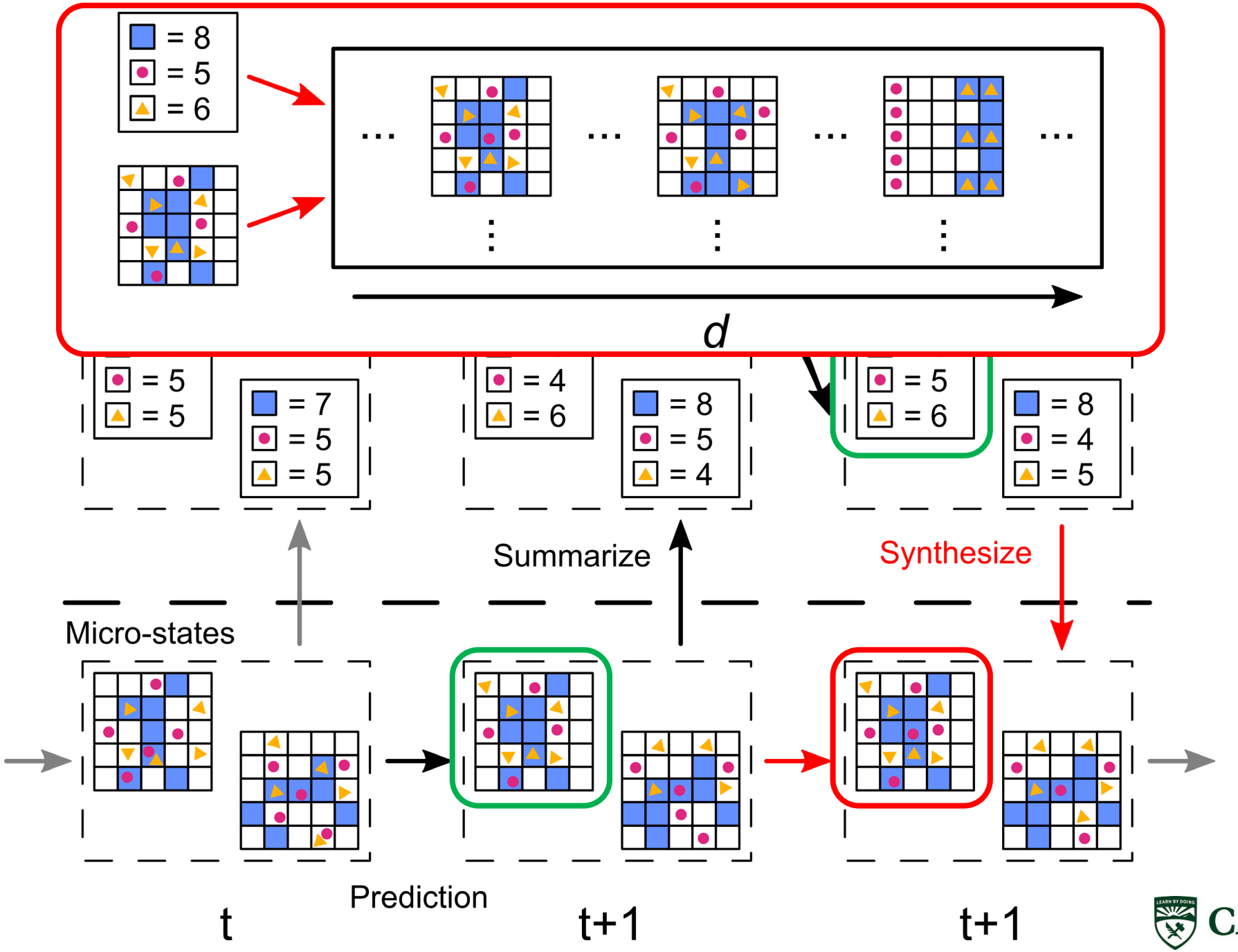
Micro-state Synthesis for ABMKF: How to choose?



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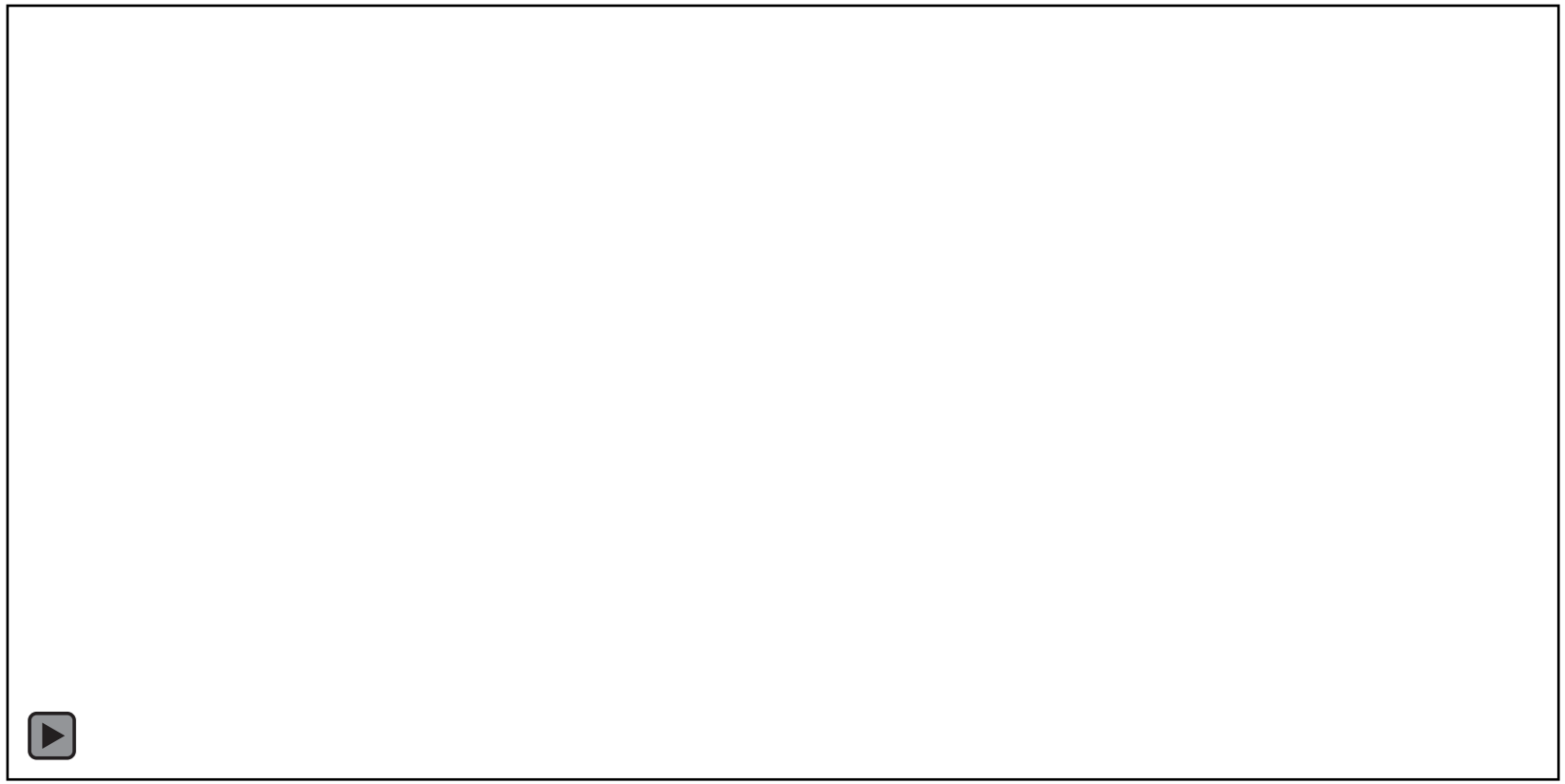
ABM of Viral Infection (Cockrell and An, 2021)

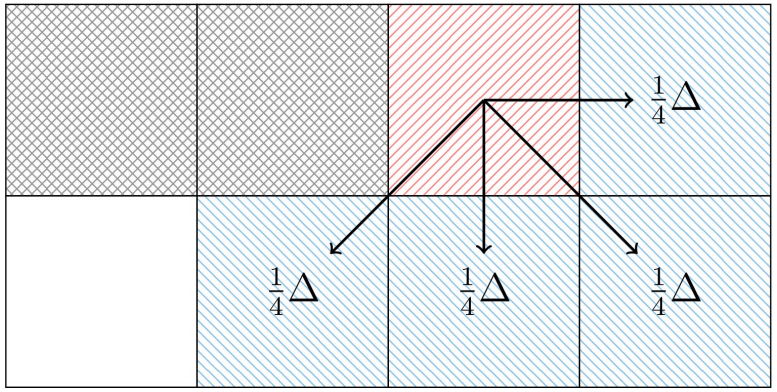


- Tissue and immune response to viral infection
- 40+ param., 20+ state variables
- 2D Healthy and Infected Epithelium

Cockrell and An 2021. Viruses. Model reimplementation in Python and simulation by A. Knapp.

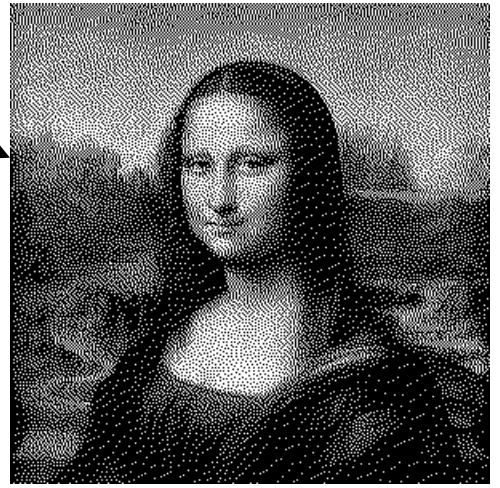
Quantization and Error Diffusion

- Quantization: The mapping of a large set to a small set
- Quantization error Δ
- Typical rounding approach can produce artifacts (“banding”)
- Error diffusion:



All colors

Black and White



Images (Right): P. Shihn. https://shihn.ca/posts/2020/dithering/

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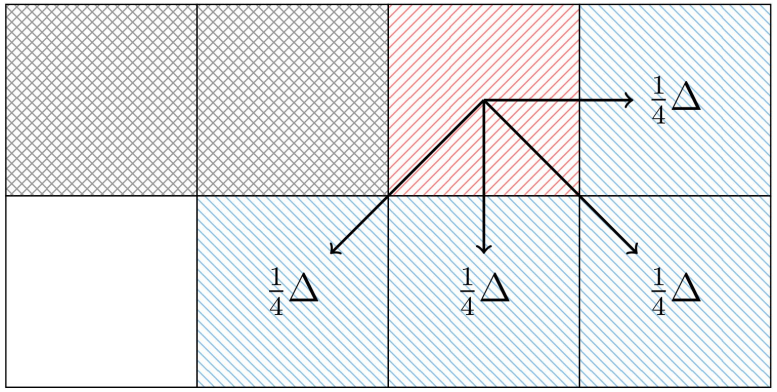
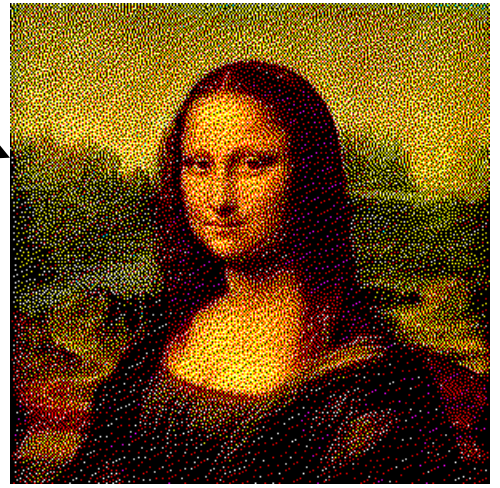


All colors

8 colors



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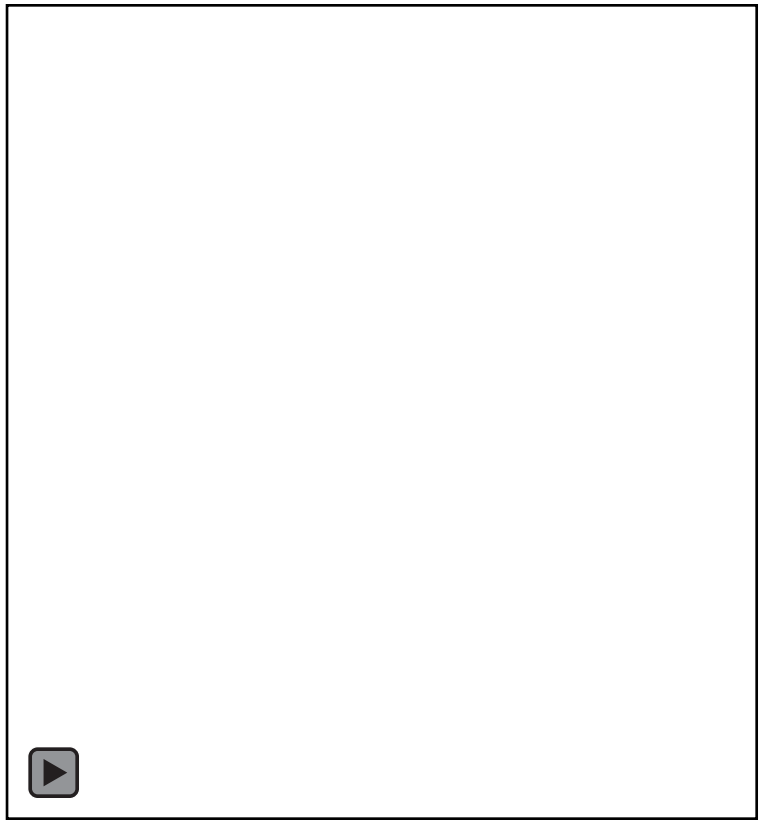
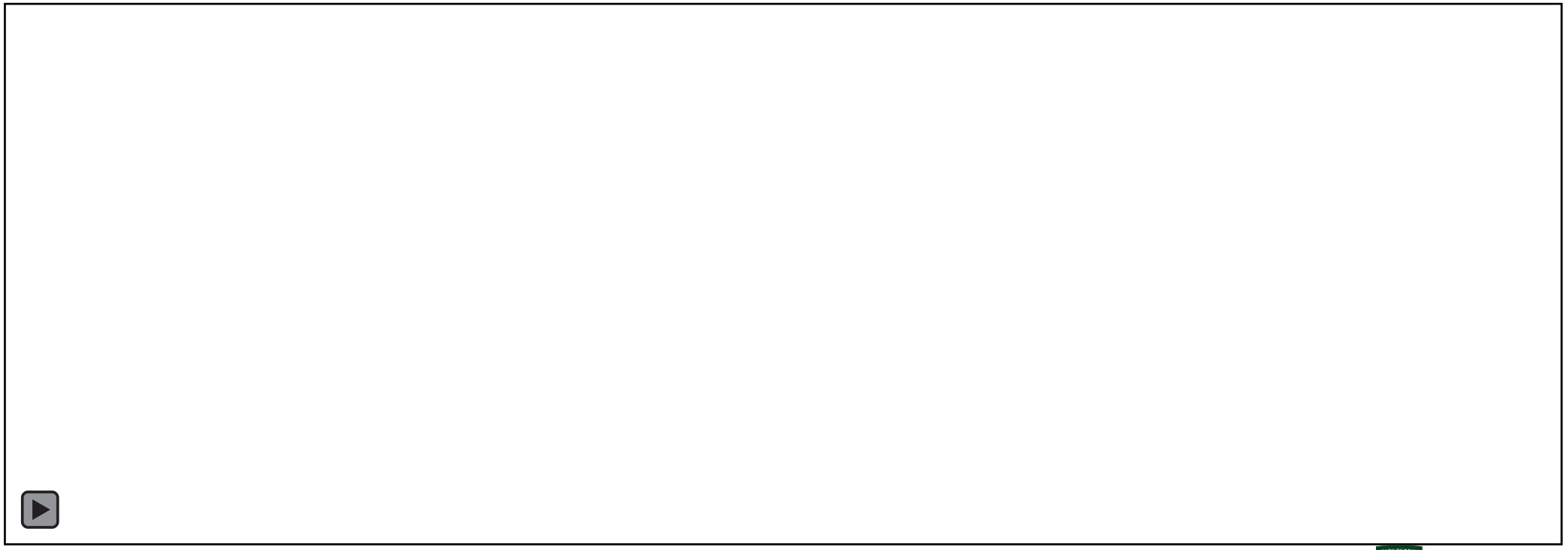
Quantization Example: Viral Infection ABM

- For continuous variables – scale up or down at each lattice point
- For discrete variables (e.g., cell state) – scale* and quantize to apply error diffusion w.r.t. the whole environment
- **Note:** The process is deterministic
  - Left to right, top to bottom
  - Other orders can be used; may produce slightly different results



Quantization Example: Viral Infection ABM

Full video by A. Knapp on YouTube



Summary and Future Work

- Summary
  - **Background:** Data assimilation (DA) and Kalman filters (KFs)
  - **Contributions:**
    - An algorithm for applying (En)KF to an ABM's macro-state as a first step example for how DA might work with stochastic, multiscale models
    - An approach for micro-state synthesis based on quantization and error diffusion techniques which respects model's spatial distribution

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- **Future Work:** Several avenues to *improve and generalize* predictions, like handling edge cases and investigating alternatives to micro-state synthesis

Thank You for Listening!

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