

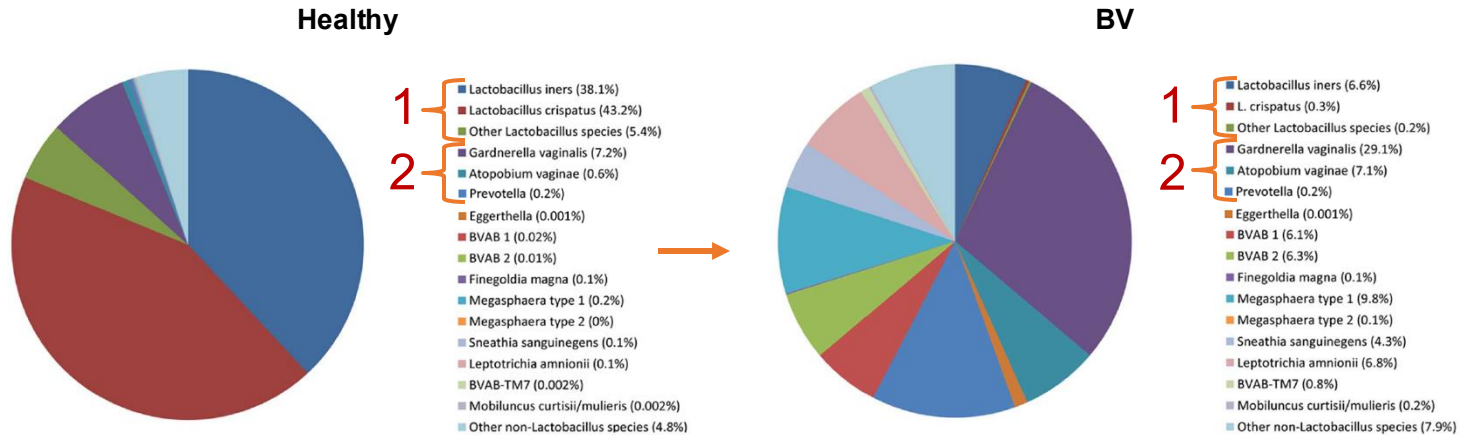
Physics-Informed Predictive Modeling of Bacterial Vaginosis Pathogen Dynamics

Bassam Fotouh, Davis Verhoeven, Hermann B. Frieboes, Ph.D.
Department of Bioengineering, University of Louisville

Clinical Challenge

Bacterial Vaginosis (BV)¹ is a dysbiotic condition of the vaginal microbiota characterized by

- Significant shift in microbiota composition.
- Lower lactic acid, hydrogen peroxide and other bacteriocins levels.

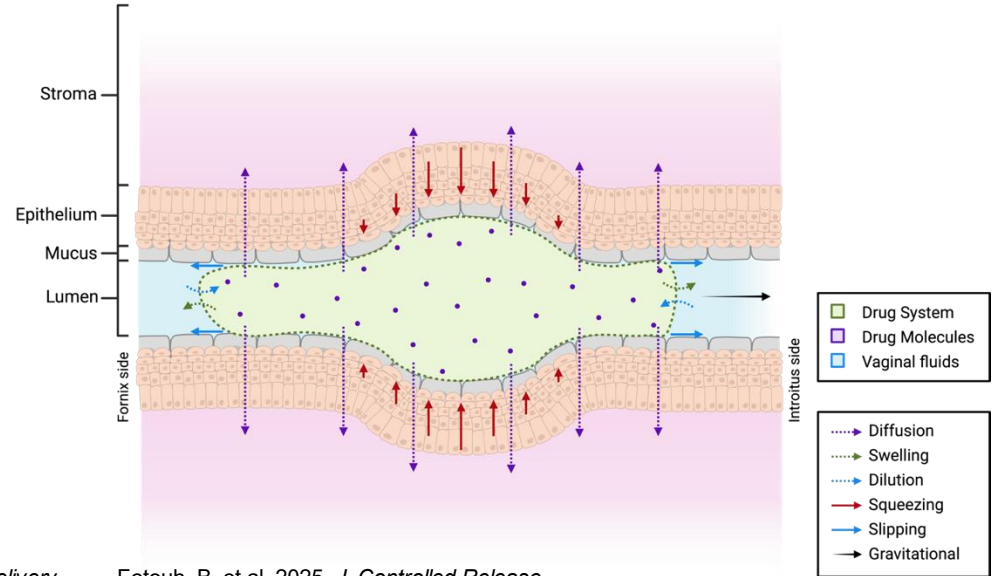
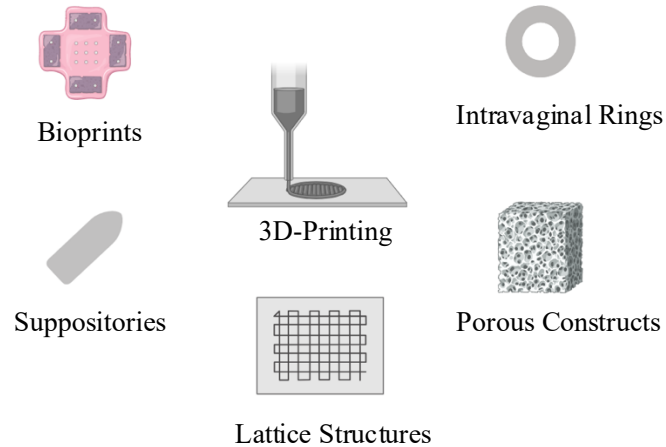


Shipitsyna, E. et al, 2013, PLoS One

1. Kumar, L. et al, 2023, Life (Basel); Rosca, A. S. et al, 2019, FEMS Microbiology Reviews.

Experimental Bottlenecks

- Preclinical animal models differ from the human vaginal milieu².
- Multivariate space: nutrients, pH, drug effects, bacterial interactions...
- Wet-lab screening = slow, costly, labor intensive



Kyser, A. et al, 2025, *Fundamentals and Future Trends of 3D Printing in Drug Delivery*

Fotouh, B. et al, 2025, *J. Controlled Release*

The Need for *in silico* Models

Reduce experimental cost and complexity by rapidly screening various scenarios².

Mathematical Modeling

- Provides Mechanistic insights.

However,

- Treats each factor in isolation.

e.g.

- Monod eq. for nutrient-limited growth.
- Logistic terms for nutrient abundance.
- Hill eq. for antibiotic kill rates,

Machine Learning (black-box predictions)

- Discovers hidden nonlinear relationships.

However,

- Needs large datasets.
- Often ignore conservation laws.
- Offer little biological insight.

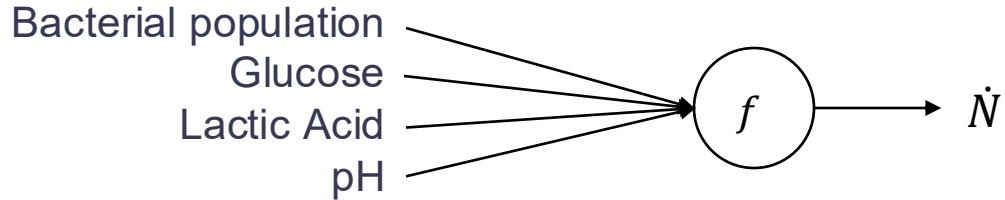
e.g.

- Neural networks.

2. Fotouh, B. et al, 2025, *J. Controlled Release*; Katz, D. et al, 2015, *Advanced Drug Delivery Reviews*.

Physics-informed Models

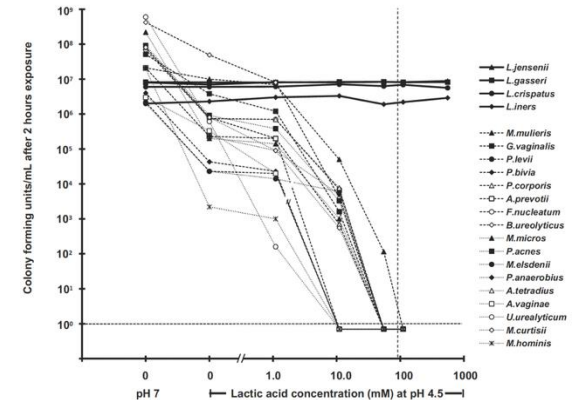
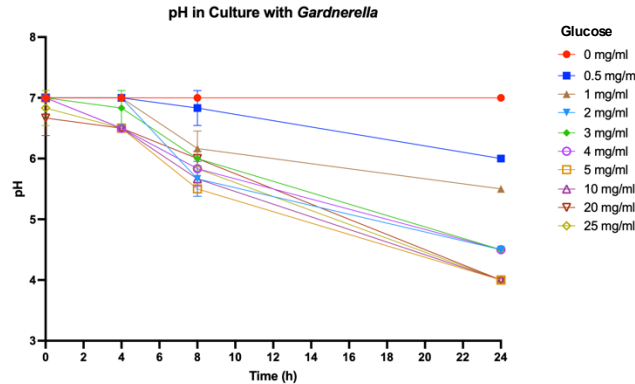
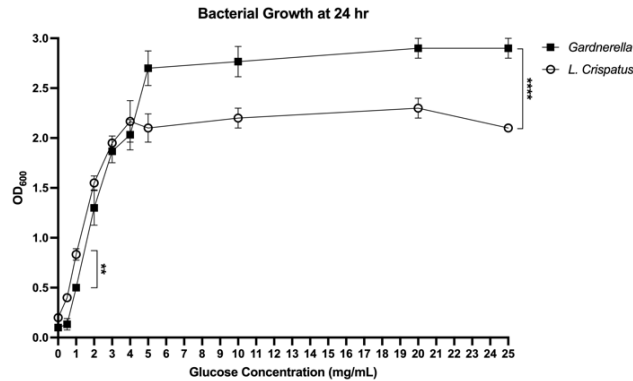
- Leverage the strengths of both mathematical modeling and machine learning.
 - Enforce physical constraints into the learning loop, yielding models that capture the dynamic nonlinear interactions while remaining interpretable³.
- **Our objective**



3. Brunton, S. L. et al, 2016, *PNAS*; Champion, K. et al, 2020, *IEEE Access*.

Preliminary Findings

- Preliminary findings along with the available literature underscore the importance of nutrient availability, pH shifts, and lactic acid-mediated suppression in dictating overall population dynamics⁴.

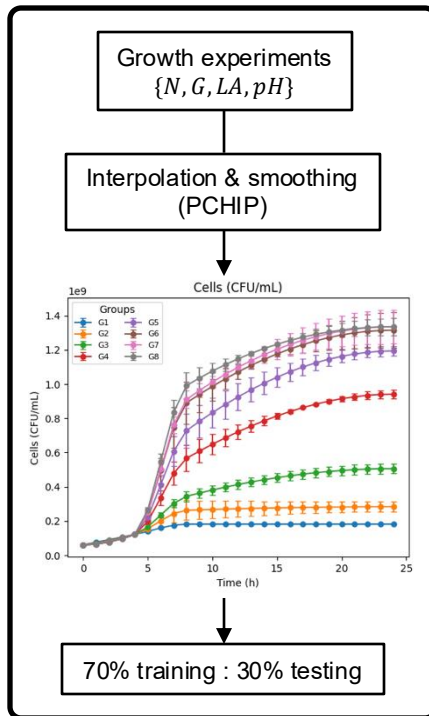


O'Hanlon, D. E. et al., 2011, *BMC Infectious Diseases*

4. Fotouh, B. et al., 2025, *Biomedical Engineering Advances*; O'Hanlon, D. E. et al., 2011, *BMC Infectious Diseases*

Modeling Framework

(a) Data & Pre-processing



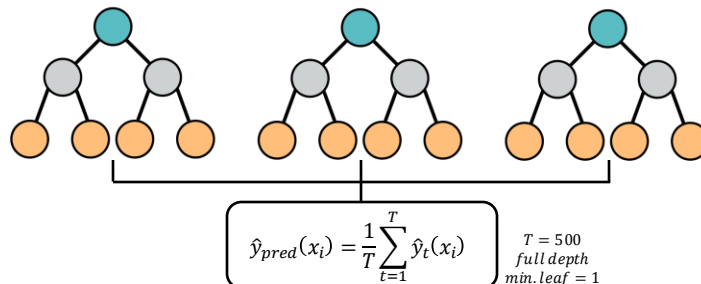
(b) Model Construction

Physics-informed learning (SINDy), constrained by mass balance & biological insights.

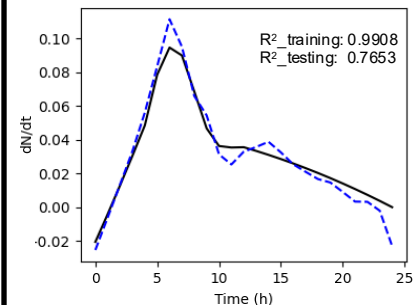
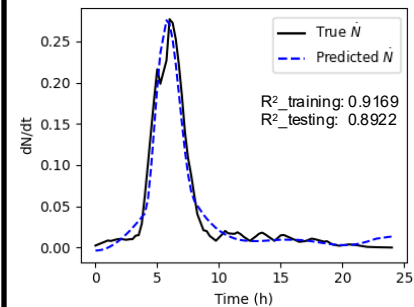
$$\begin{matrix} \dot{X} \\ \begin{bmatrix} \dot{N} \\ t_1 \\ t_2 \\ t_3 \\ \vdots \end{bmatrix} \end{matrix} = \begin{matrix} \Theta(X) \\ \begin{bmatrix} N & G & LA & pH \\ \vdots & \vdots & \vdots & \vdots \end{bmatrix} \end{matrix} \begin{matrix} \Xi \\ \begin{bmatrix} \xi \\ e_1 \\ e_2 \\ e_3 \\ \vdots \end{bmatrix} \end{matrix}$$

$$\text{SR3: } \min_{\Xi, W, v \in \Delta h} \sum_{i=1}^m \frac{1}{2} v_i \|\dot{X} - \Theta(X)\Xi\|^2 + \lambda R(W) + \frac{1}{2v} \|\Xi - W\|^2 \quad \begin{matrix} v = 1 \\ \lambda = 0.005 \end{matrix}$$

Black-box learning (Random Forest Regressor)



(c) Selection & Validation



Findings & Insights

- **Random forest (black-box) learner** shows strong in-sample fit but loses accuracy on the hold-out set, evidence of over-fitting.
- **SINDy (physics-informed) learner** delivers comparable training and testing accuracy, outperforming the black-box model on unseen trajectories.
- **Computational modeling** enables rapid *in silico* screening of pathogen behavior across multiple environmental conditions.
- **Physics-guided machine learning** benefits from mechanistic insight, providing robust predictions even under data scarcity.
- **Next steps:** extend the variable space to consider drug-bacteria and bacteria-bacteria interactions, and embed the learned model into a predictive framework for drug optimization.

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Thank you!