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Microbiology PERSPECTIVE

From virtual cells to virtual bacteria — Towards the era of evolvable micro-life digital twins

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Life sciences are entering a stage where computational modeling and experimental biology are deeply intertwined, giving rise to the concept of digital twins in living systems. This perspective outlines the transition from virtual cells toward dynamic virtual bacteria—a new framework that seeks to reconstruct prokaryotic life in silico with evolutionary and adaptive capability. By integrating genomic, metabolic, and biophysical data, Virtual Bacteria models aim to replicate bacterial behavior, community interactions, and evolutionary dynamics at multiple scales. However, this transition requires addressing significant computational bottlenecks, data gaps in genetic understanding, and ethical governance. Such systems hold broad potential for synthetic biology, microbial ecology, antibiotic resistance research, and the study of host–microbiome relationships. Beyond their practical utility, they also offer a novel platform for exploring the origin and evolution of life from a computational standpoint. Establishing evolvable digital micro-life will not only deepen our understanding of biological complexity but may also reframe how science conceptualizes and experiments with living systems in the coming digital era.

Over the past decade, life sciences have undergone a profound transformation in which computational analysis and experimental biology are becoming inseparable. The rapid evolution of bioinformatics, molecular modeling, and systems biology now allows researchers to reconstruct living cells across multiple scales.[1] Significant milestones, such as the whole-cell model of *Mycoplasma genitalium* and extensive Genome-Scale Metabolic Models (GEMs), have successfully captured static snapshots of cellular function or specific metabolic fluxes. Such progress has given rise to concepts like "virtual cells" and "virtual organoids," enabling observation of biological complexity within a digital environment.[2,3] However, these existing frameworks often lack the capacity for multi-generational adaptation.[4] They represent a "read-only" state of biology, whereas the next frontier requires "read-write-evolve" capabilities.

Bacteria represent the earliest and most ubiquitous form of life on Earth.[5] Exploring bacterial mechanisms through a dynamic virtual framework can provide insights into metabolic regulations, evolutionary adaptation, and resistance mechanisms—all fundamental to understanding life and advancing biotechnology. This perspective introduces the concept of Virtual Bacteria, a digital modeling framework designed to create operational and evolvable virtual microorganisms. It aims to extend biological modeling from static representation to continuous simulation of living processes capable of dynamic change (Figure 1).

FROM PARTIAL STIMULATION TO HOLISTIC RECONSTRUCTION: THE SCIENTIFIC ESSENCE OF VIRTUAL BACTERIA

Virtual Bacteria is not merely a collection of molecular data or computational codes; it is an integrative modeling philosophy grounded in quantitative systems biology. Its overarching goal is to recreate the entire life cycle of bacterial organisms within a virtual environment. Unlike traditional GEMs, which optimize for steady states, Virtual Bacteria models must synthesize genetic information, biochemical reactions, and structural mechanics in a coherent, time-dependent manner to allow for emergent behaviors.

Within such a system, the genome, transcriptome, proteome, and metabolome are connected through dynamic equations that describe the interactions among genes, enzymes, and metabolites. Crucially, to achieve "evolvability," the system requires a Virtual Evolutionary Engine. This module introduces stochasticity into DNA replication fidelity, simulating mutation rates and horizontal gene transfer events. By coupling genotype changes to quantitative phenotype outputs (e.g., growth rate, thermal tolerance), the model can compute fitness landscapes dynamically under varying selection pressures. Equally important is the physical representation of bacterial structure. A credible virtual model must account for cellular membrane elasticity, wall rigidity, osmotic pressure, and motion mechanics sustaining bacterial survival. At the population level, the true complexity of bacterial life emerges.[6] A functioning Virtual Bacteria ecosystem should allow these behaviors to appear spontaneously within digital space via Agent-Based Modeling (ABM), permitting virtual organisms to communicate, compete, and evolve.

METHODOLOGICAL PATH AND IMPLEMENTATION CHALLENGES

Realizing Virtual Bacteria requires a hybrid computational architecture. We propose a multi-layer framework where Ordinary Differential Equations (ODEs) resolve rapid intracellular metabolic fluxes, while Agent-Based Models (ABM) handle population-level interactions and evolutionary selection. Bridging these scales requires advanced Machine Learning (ML) algorithms to approximate complex biophysical dynamics without prohibitive computational costs.

However, significant hurdles remain. First is the "Dark Matter" of the genome. Human knowledge has not yet uncovered the function of all genetic elements, and mechanistic understanding of many biochemical interactions remains incomplete. To address this, we must build comprehensive, curated databases of microbial interactions and utilize AI to infer potential functions of unknown genes, iteratively validating these predictions against wet-lab data. Second is the computational load. Simulating an evolving colony at molecular resolution demands exascale computing power currently beyond standard reach. Future implementations may require distributed cloud computing or quantum algorithms to manage the combinatorial explosion of evolutionary trajectories. Model verification is a critical component. A robust Virtual Bacteria system must maintain an iterative feedback loop between simulation and experiment. This closed cycle transforms modeling into a self-correcting scientific process where computation and empirical observation advance reciprocally.

RESEARCH SIGNIFICANCE AND POTENTIAL APPLICATIONS

The scientific and technological implications of Virtual Bacteria are far-reaching. In synthetic biology, the design–build–test–learn engineering loop often consumes substantial resources. Simulating genetic circuits within virtual bacterial models could optimize design strategies before any laboratory experiment is conducted. This "in silico prototyping" would not only accelerate experimental throughput but also minimize trial and error, enhancing reproducibility and cost-efficiency.

In the ongoing fight against antibiotic resistance,[7] a Virtual Bacteria platform could prove indispensable. Resistance evolution is driven by complex interactions among mutation, selection pressure, and horizontal gene transfer—processes that are difficult to capture experimentally. Through computational modeling, one could simulate bacterial adaptation under drug exposure, and evaluate strategies to counter their spread.

ETHICAL AND BIOSECURITY IMPLICATIONS

While Virtual Bacteria offer immense benefits, they introduce dual-use risks that must be acknowledged. The same tools used to predict antibiotic resistance could theoretically be employed to design hyper-resistant pathogens or optimize toxin production. As the fidelity of these digital twins improves, governance frameworks must be established. This includes strictly regulating access to "pathogenic kernels" within the code and establishing ethical guidelines for the creation and deletion of digital life forms, ensuring that these simu-

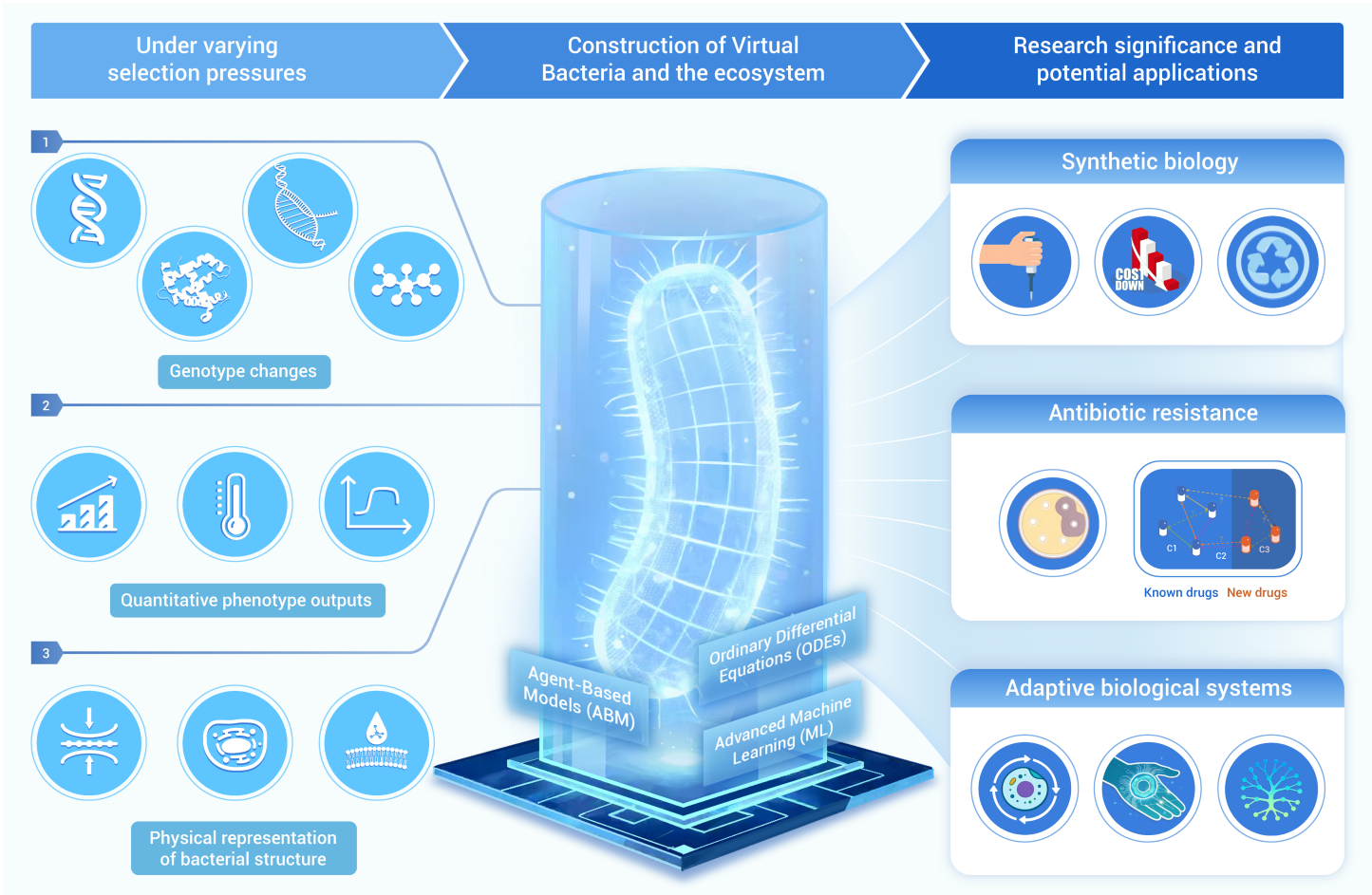

Figure 1. Construction of virtual bacteria and associated ecosystem, with research significance and potential applications.

lations serve potential public health goals without compromising biosecurity.

INTEGRATION OF THEORY AND REALITY: FUTURE OUTLOOK

The advent of Virtual Bacteria implies more than a technological innovation—it symbolizes a paradigm shift in life science methodology. It extends experimentation beyond the physical laboratory. As fidelity and complexity improve, these digital organisms could coalesce into larger-scale ecosystems, forming virtual microbial communities capable of nutrient cycling, energy exchange, and co-evolution.

In a broader context, Virtual Bacteria accentuates the convergence of theoretical biology, synthetic science, and bioethics. The ability to simulate adaptive biological systems might expand what constitutes "life" in scientific discourse—suggesting that the boundary between the living and the digital is not strict but continuously evolving.

CONCLUSION

Though life's complexity often appears overwhelming, understanding begins with its simplest manifestations. Bacteria remain the key to deciphering life's core principles. Constructing Virtual Bacteria represents not only a technological challenge but also a scientific opportunity.

By establishing multi-level models linking genes, biochemistry, structure, and ecology, researchers can move from passive observation to active recreation of biological phenomena. When virtual bacterial colonies begin to grow, compete, and evolve in computational space, biological understanding will take on a new dimension. The emergence of evolvable micro-life digital twins may ultimately reshape the mission of the life sciences—not merely to study life, but to rebuild and reinterpret it within the framework of an ever-expanding digital universe.

REFERENCES

1. Cui T., Zhou Y. and Wang T. (2025). Recent advances in artificial intelligence-driven biomolecular dynamics simulations based on machine learning force fields. *Curr. Opin. Struct. Biol.* **95**:103191. DOI:10.1016/j.sbi.2025.103191
2. Bunne C., Roohani Y., Rosen Y., et al. (2024). How to build the virtual cell with artificial intelligence: Priorities and opportunities. *Cell* **187**:7045–7063. DOI:10.1016/j.cell.2024.11.015
3. Bai L. and Su J. (2026). Artificial intelligence virtual organoids (AIVOs). *Bioact. Mater.* **59**:45–68. DOI:10.1016/j.bioactmat.2025.12.030
4. Zhou L., Chen S., Liu J., et al. (2025). When artificial intelligence (AI) meets organoids and organs-on-chips (OoCs): Game-changer for drug discovery and development. *Innov. Life* **3**:100115. DOI:10.59717/j.xinn-life.2024.100115
5. Davín A. A., Woodcroft B. J., Soo R. M., et al. (2025). A geological timescale for bacterial evolution and oxygen adaptation. *Science* **388**:6742. DOI:10.1126/science.adp1853
6. Liu S., Feng X., Zhang H., et al. (2025). Decoding bacterial communication: Intracellular signal transduction, quorum sensing, and cross-kingdom interactions. *Microbiol. Res.* **292**:127995. DOI:10.1016/j.micres.2024.127995
7. GBD 2021 Antimicrobial Resistance Collaborators (2024). Global burden of bacterial antimicrobial resistance 1990-2021: A systematic analysis with forecasts to 2050. *Lancet* **404**:1199–1226. DOI: 10.1016/S0140-6736(24)01867-1

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AUTHOR CONTRIBUTIONS

Zhexin Ni and Wei Zhou wrote the manuscript. Yue Gao proposed the concept and reviewed the manuscript. All authors contributed to the manuscript and approved the final version.

DECLARATION OF INTERESTS

The authors declare no competing interests.