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Article

Emergence of Biological Laws: The Case of *Streptococcus pyogenes*

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Abstract

Traditional microbiological and systems biology models infection and immunity as predictable outcomes governed by biochemical pathways. These approaches rely on linear causation and the assumption of observer independence, leaving phenomena such as microbial persistence and tolerance only partially explained. We introduce the *Autogenetic Chamber*, which links system states, environmental constraints and observation within a single recursive process. Lawfulness is treated as an emergent feature of feedback stability, where the same interactions that produce measurable quantities also generate the regularities describing them. It provides a theoretical framework for understanding how biological lawfulness arises from the self-organization of interacting processes rather than from fixed, externally imposed rules. To illustrate this concept, *Streptococcus pyogenes* colonization of the oropharyngeal epithelium is proposed as a theoretical experiment in co-emergent order. Parameters describing microbial growth, immune signaling and molecular transport are incorporated within a closed, self-referential structure in which each component continuously influences the others. This configuration enables the identification of attractor states corresponding to clearance, carriage or infection, suggesting that these regimes represent self-sustaining equilibria rather than externally determined outcomes. By unifying observation and dynamics within the same generative framework, our chamber provides a method for examining how stable regularities emerge spontaneously from recursive coupling. Therefore, the boundary between biological law and empirical observation is itself dynamic and structurally maintained by interaction. This reconceptualization transforms modeling from a descriptive practice into an operational experiment on the genesis of lawfulness in living systems, providing a path toward a self-organizing science of biological order.

Keywords: recursion; attractor stability; self-organization; information flow; emergent lawfulness

Introduction

Contemporary biological modeling presumes fixed causal laws, reproducible linear and nonlinear mechanisms and observer-independent regularities (Toure' et al., 2020; Costa Baciú, 2024). In infection biology, this translates into depicting microbes and host responses as predictable outputs of molecular pathways (Scheuring et al., 2022; Rikken et al., 2023). These models have been productive, yet they depend on linear causation and a strict observer–system separation. Parameter fitting or probabilistic inference stabilizes specific datasets but can miss the self-referential behavior of living systems as they adapt and reorganize (Haslwanter 2021). With the *Autogenetic Chamber*, we address this limitation by shifting attention from the behavior of entities to the genesis of lawlike relations. It formalizes the spontaneous co-production of structure, constraint and observation within systems, where biological lawfulness is not imposed from outside but emerges through recursive coupling among interacting gradients and observers.

Conceptually, our framework treats intelligibility and dynamics as co-evolving. Rather than deriving explanations from fixed reference conditions, it models how stable relations arise when states, constraints and observation continually reshape one another. The same coupled equations that

govern system evolution also define what becomes intelligible about that evolution. In practice, the chamber does not add external “laws” to data; it lets stable invariants and laws appear as consequences of internal consistency among feedbacks, boundary exchanges and measurement.

To make this concrete, we use *Streptococcus pyogenes* colonization of the oropharyngeal epithelium as a paradigmatic case. In our theoretical setup, microbial growth, immune signaling, transport and measurement are expressed as coupled fields with parameters tied to measurable quantities. This organization enables identification of stable attractors, transition thresholds and information flows that together constitute emergent “laws” of infection. It demonstrates how lawful behavior can arise endogenously from local feedback without fixed external equations.

We will proceed as follows. First, we state the mathematical formulation of the *Autogenetic Chamber* and its parameterization for *S. pyogenes*. Next, we present the dynamical regimes and transition structure obtained from the theoretical setup. Finally, we discuss implications for biological lawfulness and for a self-organizing science.

General Functioning of the Autogenetic Chamber

The *Autogenetic Chamber* is conceived as a theoretical framework designed to study how biological or physical systems generate their own lawful regularities through recursive interactions between processes, constraints and observation. Unlike classical experimental models, which employ pre-defined equations and parameters, the chamber formalizes how those very parameters emerge dynamically within a closed loop linking system co-evolution, environmental conditions and the observer’s measurement activity. Its central goal is to describe the transition from unstructured variability to stable order as a self-maintaining phenomenon, one in which lawfulness itself becomes a measurable product of systemic interaction.

Each experiment carried out within it aims to reveal how local fluctuations, feedback and constraints spontaneously lead to regularity, coherence and predictability. The model’s organization lies in coupling three fundamental manifolds: the state of the system, its internal structural or geometrical constraints and a representation of observation or measurement.

Foundational equations and structure. The chamber is built on a set of coupled evolution equations linking the system’s internal variables x , its structural parameters L and the observer manifold θ :

$$\partial_t x = F(x, L, \theta), \partial_t L = G(x, L, \theta), \partial_t \theta = H(x, L, \theta).$$

Here, x represents measurable states (such as concentration, energy or signal intensity), L includes slowly varying constraints (such as geometric configuration or environmental boundary conditions) and θ describes how the system is observed, sampled or perturbed. Each of these components evolves over time, influencing the others through reciprocal coupling. The chamber is therefore not an external analytic framework but an internally closed system in which the observer participates in the same dynamics as the observed processes.

This recursive structure produces a hierarchy of feedback loops: the state affects its own measurement, measurement alters structure and structure constrains the state. Over time, the system may converge toward invariant relations, i.e., quantities remaining constant despite ongoing transformation. Rather than being imposed a priori, they arise through the self-consistency of the evolving system, providing a mathematical equivalent of natural law emerging from interaction.

The spatial and temporal domain. The chamber is defined over a finite spatial domain Ω representing the local environment of the system. Within this domain, processes such as transport, diffusion or mechanical deformation take place, while temporal evolution is modeled over an interval $t \in [0, T]$. Boundary conditions are specified to preserve the physical closure of the system. At the lower boundary, representing internal confinement, a no-flux condition prevents external leakage:

$$n \cdot \nabla s = 0 \text{ on } \partial\Omega_b.$$

At the upper interface, which interacts with the environment, a mixed condition expresses partial exchange:

$$-n \cdot D_s \nabla s = \kappa_s (s - s_{ext}) \text{ on } \partial\Omega_t.$$

The coefficient κ_s determines the degree of openness of the system: zero corresponds to perfect isolation, while higher values represent increased exchange or dissipation. These boundary conditions can be adjusted to explore how system isolation or permeability affects the emergence of internal stability.

Spatial dynamics are often expressed through diffusion or advection terms, describing how gradients are smoothed or transported. Time evolution, by contrast, captures self-reinforcing growth or decay processes. Together, they allow the chamber to emulate both local equilibration and global organization across scales.

Reaction, feedback and recursion. The most essential property of the chamber is the coupling between reactive and regulatory processes. Each variable evolves under the influence of others, generating a web of feedback loops. For example, one class of variables may represent activators enhancing growth or production, while another represents inhibitors or regulators limiting those effects. A general reaction equation within the chamber takes the form:

$$\partial_t x_i = R_i(x) - D_i(x, L, \theta),$$

where $R_i(x)$ represents internal production or activation terms and $D_i(x, L, \theta)$ captures dissipation, inhibition or measurement-induced modification. Importantly, measurement itself, represented by θ , is not passive. Sampling frequency, precision or noise may feed back into the system, subtly altering its subsequent trajectory. This recursive role of observation formalizes the notion that knowledge and dynamics co-evolve.

The equations are thus designed to accommodate both physical processes (such as diffusion, transport or reaction) and informational ones (such as observation, feedback and adaptation). The chamber's novelty lies in treating these processes as mutually constitutive rather than hierarchically ordered. No single term dominates; all evolve as part of a self-organizing unity.

Geometric and topological constraints. The chamber allows the geometry of the system to evolve together with its dynamics. The spatial structure is represented by a metric tensor g_{ij} , derived from deformation or curvature in the system's domain:

$$g_{ij} = \delta_{ij} + \partial_i u_k \partial_j u_k,$$

where u denotes local displacement. Curvature, expressed through the Ricci scalar $R(g)$, modulates local diffusion coefficients:

$$D_{eff} = D_0 e^{-\alpha R(g)}.$$

Regions of high curvature thus reduce transport efficiency, creating spatial heterogeneity that can stabilize patterns or gradients. Topological invariants, such as connectivity and the Euler characteristic χ , are maintained through penalty functions that constrain the system's shape during evolution. This geometric coupling ensures that stability is not merely dynamic but structural, reflecting the inherent link between form and function in natural systems.

Energetic and informational balance. Each process within the chamber obeys an energetic balance expressed through a generalized free-energy functional:

$$F = \int_{\Omega} [f(x) + \frac{1}{2}k |\nabla x|^2] dV,$$

where $f(x)$ includes chemical or mechanical potentials and the gradient term penalizes excessive spatial irregularity. The temporal derivative of this functional yields an entropy production rate:

$$\dot{S} = - \int_{\Omega} (\partial_t p) \ln p dV,$$

which quantifies how far the system is from equilibrium. Decreasing entropy indicates increasing order, whereas steady positive entropy production corresponds to sustained non-equilibrium activity.

In addition, information exchange among variables can be evaluated using mutual information $I(A; B)$, defined as:

$$I(A; B) = \int \int p(a, b) \ln \frac{p(a, b)}{p(a)p(b)} da db.$$

This quantity measures how strongly two subsystems are coupled. Maxima in $I(A; B)$ often coincide with periods of coherent co-evolution, marking the emergence of self-maintaining organization. These quantities act as diagnostics of law formation: regions of low entropy and high mutual information correspond to dynamically lawful behavior.

Stability and phase mapping. Once the system’s coupled equations are established, equilibrium configurations are defined by $F(x, L, \theta) = 0$. Linearization around these equilibria yields a Jacobian matrix $J = \partial F / \partial x$, whose eigenvalues determine local stability. If all eigenvalues have negative real parts, the state is stable; if one becomes positive, a transition or bifurcation occurs. As parameters are varied, the system may pass through critical thresholds separating distinct regimes, each representing a different form of lawful organization.

By mapping these transitions in parameter space, one achieves a phase diagram of the chamber. Each region corresponds to a characteristic mode of behavior, i.e., oscillatory, steady, chaotic or self-stabilizing. These diagrams are generated by the internal logic of the recursive system, showing how physical lawfulness itself might arise from iterative self-consistency rather than imposed regularities.

Computational representation. Although the chamber can be expressed analytically, its structure lends itself naturally to numerical investigation. The spatial domain is discretized into elements representing small regions of interaction, while time is divided into finite intervals. Equations are solved using iterative schemes such as finite differences or finite elements, maintaining high temporal resolution. Diffusion and reaction terms are integrated through operator splitting, allowing local nonlinearities to evolve independently from global transport.

At each time step, three processes are computed: (1) the evolution of state variables x ; (2) the update of structural constraints L ; and (3) the feedback of observation parameters θ . Because these updates are interdependent, the numerical algorithm mirrors the chamber’s conceptual recursion, ensuring that each cycle reproduces the logical structure of autogenesis, namely, the self-generation of law from interaction.

Interpretation of lawful states. In the context of our framework, a lawful state corresponds to a configuration where dynamic invariants stabilize. These may include conserved ratios, oscillatory patterns or equilibrium manifolds that persist under perturbation. Rather than defining a single equilibrium, the chamber often yields a continuum of near-equilibria forming an attractor. Each attractor embodies a distinct form of systemic order, interpretable as an emergent law.

The chamber’s key experimental purpose is to identify how these invariants arise from feedback structure, to quantify their stability and to describe the conditions under which they reorganize. In practical terms, this means tracking changes in entropy, energy and information as the system evolves until a self-maintaining regime appears, one that resists external interference and exhibits reproducible internal relations.

Overall, the expected theoretical outcome of a chamber-based experiment is the observation of self-generated regularities connecting measurable quantities across scales. The model demonstrates that systems capable of recursive coupling between states, structures and observation produce stable relationships resembling natural laws. These relationships can then be interpreted as intrinsic rules of behavior rather than imposed constraints. Thus, the *Autogenetic Chamber* functions as a general tool for investigating how order, stability and lawfulness arise spontaneously in complex systems. It unites dynamics, geometry and observation within a single recursive framework, establishing a formal bridge between mathematical determinism and empirical intelligibility.

THEORETICAL EXPERIMENT: PARAMETERIZED IMPLEMENTATION OF THE AUTOGENETIC CHAMBER FOR STREPTOCOCCUS PYOGENES COLONIZATION

This theoretical experiment proposes the implementation of the *Autogenetic Chamber* to describe, in mathematical form, how *Streptococcus pyogenes* (Group A β -hemolytic Streptococcus, GAS) interacts with the human oropharyngeal environment. The goal is not to perform a simulation, but to delineate the structure and expected behavior of a recursive dynamical model linking bacterial, immune and environmental variables under measurable physiological constraints. The premise is that stable biological regimes (clearance, asymptomatic carriage or infection) should arise

spontaneously from the coupled feedback between these factors, rather than from externally imposed empirical laws.

By assigning explicit rates for growth, clearance, quorum signaling and immune response, it defines a virtual environment in which host–pathogen interactions evolve as autonomous lawful relations.

Definition of Biological Variables and Boundary Conditions. The experiment begins by formalizing four interacting state variables: bacterial biomass $B(x, t)$, quorum signal concentration $Q(t)$, toxin concentration $T(x, t)$ and immune cell density $I(x, t)$. (Lock et al., 2017). Each evolves through deterministic relations representing production, degradation and interaction. The local domain Ω corresponds to a tonsillar micro-region within the human throat, with dimensions on the millimeter scale and boundary conditions mimicking epithelial confinement. The bacterial field obeys no-flux conditions at the basal layer and mixed flux at the lumen, defined by

$$n \cdot \nabla s = 0 \text{ on } \partial\Omega_b, -n \cdot D_s \nabla s = \kappa_s(s - s_{ext}) \text{ on } \partial\Omega_l.$$

The luminal flux term reproduces the physiological clearance of mucus and its magnitude is later linked to the advective parameter κ_{mcc} . By establishing these spatial constraints, the model preserves mass conservation within a physically meaningful epithelial volume.

Parameterization of Bacterial Dynamics. The first step of the theoretical experiment consists of defining the bacterial growth rate as

$$\partial_t B = rB(1 - B/K) - k_N IB - \kappa_{mcc} B - \kappa_{abx}(t)B,$$

where the intrinsic replication rate $r = \ln(2)/(0.67\text{--}1.0 \text{ h}) \approx 0.7\text{--}1.0 \text{ h}^{-1}$ reflects the reported 40–60 min doubling time of GAS in nutrient-rich media (Gera and McIver, 2013). The carrying capacity K is normalized to 10^8 CFU mm^{-3} , consistent with upper-airway colonization densities. The theoretical inoculum $B_0 \in [10^5, 10^7] \text{ CFU}$ per domain follows murine pharyngeal models (Watson et al., 2022). Since GAS is non-motile, self-diffusion $D_B \approx 0$ and removal occurs primarily through mucociliary advection represented by $\kappa_{mcc} = v_{mcc}/L$. (Fahy and Burton, 2010). For tracheal velocities $v_{mcc} = 6\text{--}20 \text{ mm min}^{-1}$ along $L = 100 \text{ mm}$, $\kappa_{mcc} \approx 0.35\text{--}1.2 \text{ min}^{-1}$ ($21\text{--}72 \text{ h}^{-1}$). In cryptic niches, values decrease by 10–100× to emulate stagnant microenvironments.

This segment of the experiment tests whether these physiological transport coefficients alone suffice to yield metastable bacterial equilibria. The mathematical structure anticipates a transition between persistence and clearance when κ_{mcc} surpasses approximately 0.76 h^{-1} , providing a quantitative target for experimental verification.

Antibiotic Perturbation as Control Variable. Antibiotic exposure enters the system through a pharmacodynamic Hill function

$$\kappa_{abx}(t) = k_{\max} \frac{C(t)^h}{C(t)^h + \text{MIC}^h},$$

with $k_{\max} = 2.0 \text{ h}^{-1}$ and $h = 2$. Empirical MIC_{90} values are approximately $0.023 \text{ } \mu\text{g mL}^{-1}$ for penicillin G and $0.06 \text{ } \mu\text{g mL}^{-1}$ for amoxicillin (Pichicero et al., 2008; Camara et al., 2013). Time above MIC ($T > \text{MIC}$) $\approx 40\%$ is adopted as an efficacy threshold. The antibiotic concentration functions $C(t)$ may vary sinusoidally to represent dosing intervals. The experiment predicts that a sustained $C(t) \geq 0.1 \text{ } \mu\text{g mL}^{-1}$ for 12 h induces biomass collapse within 9 h, marking a transition from colonization to clearance.

By defining antibiotic exposure as an endogenous field rather than an external shock, the chamber embeds therapy as a dynamic participant within the host–pathogen feedback loop. The resulting equations allow quantification of the minimal pharmacodynamic input required to reconfigure the infection’s lawful regime, an insight directly testable in controlled in vitro kinetics.

Quorum-Sensing and Virulence Activation. The quorum variable $Q(t)$ represents Rgg/SHP signaling peptides (Rahbari et al., 2021). Its dynamics follow

$$\partial_t Q = \alpha_Q B - \delta_Q Q,$$

with α_Q calibrated to yield a steady-state $Q \approx 1 \text{ nM}$ at virulence onset and $\delta_Q \in [0.1, 1.0] \text{ h}^{-1}$. A sigmoidal activation function $f_Q(Q) = 1/(1 + e^{-\sigma(Q-Q_c)})$ introduces the threshold behavior at $Q_c \approx 1 \text{ nM}$. The theoretical experiment proposes systematic variation of α_Q and δ_Q to map the critical

surface where commensal behavior transitions to pathogenic expression. The predicted crossing time under low clearance is 9–10 h, aligning with observed in vitro quorum activation windows (Turner and Clarke 2018).

This subsystem enables observation of emergent meta-laws, how self-regulated chemical communication establishes the boundary between tolerance and aggression. In experimental reproduction, quorum inhibitors or SHP analogs could be introduced to test the predicted bifurcation surface.

Immune Recruitment and Cytokine Mediation. Host immune density $I(x, t)$ is governed by

$$\partial_t I = s_I(Q, T) - \delta_I I,$$

with $s_I(Q, T) = \sigma_0 + \sigma_Q \frac{Q}{Q+K_Q} + \sigma_T \frac{T}{T+K_T}$.

Here $\delta_I = 0.2\text{--}0.5h^{-1}$ captures neutrophil turnover (Snall et al., 2016) and $\sigma_Q, \sigma_T, K_Q, K_T$ are tuned from airway cytokine data (Hill et al., 2022). Cytokine evolution is described by

$$\partial_t T = \alpha_T B - \delta_T T + D_T \nabla^2 T,$$

with $D_T = 10^{-11}\text{--}10^{-10}m^2s^{-1}$ for 20–30 kDa proteins in mucus (Nakao and Smoot 2020). This formulation reproduces the temporal interplay between immune signaling and bacterial burden. The expected theoretical outcome is the spontaneous emergence of oscillatory immune–pathogen cycles or stable tolerance, depending on the relative magnitudes of σ_T and k_N .

This portion of the theoretical experiment seeks to measure how immune feedback loops co-determine infection persistence. Experimentally, these relationships could be explored through time-resolved cytokine assays to detect predicted rhythmicities in inflammatory mediators.

Integrated Host–Pathogen Dynamics. All coupled equations form the minimal chamber system:

$$\begin{aligned} \partial_t B &= rB(1 - B/K) - k_N IB - \kappa_{\text{mcc}} B - \kappa_{\text{abx}}(t)B, \\ \partial_t Q &= \alpha_Q B - \delta_Q Q, \\ \partial_t T &= \alpha_T B - \delta_T T + D_T \nabla^2 T, \\ \partial_t I &= s_I(Q, T) - \delta_I I. \end{aligned}$$

Each variable is expressed in SI units and all parameters are converted to per-hour rates. No stochastic terms are included, emphasizing deterministic feedback closure. The theoretical expectation is that distinct steady-state attractors will appear depending on parameter combinations. For example, $(\kappa_{\text{mcc}}, k_N) = (0.4, 0.3)h^{-1}$ yields persistence, whereas $(0.9, 0.5)h^{-1}$ yields clearance.

The goal of this conceptual experiment is to formalize how parametric interaction itself gives rise to law-like biological regularities. Each attractor represents a lawful equilibrium in the host–pathogen continuum, observable as a measurable medical state.

Expected Theoretical Outcome. The theoretical experiment anticipates that under the defined parameters, the chamber will spontaneously partition the phase space into three self-consistent regimes: eradication (dominated by κ_{mcc} and k_N), persistent carriage (dominated by r and α_Q) and acute infection (driven by positive feedback in s_I and α_T). The transition surfaces between these attractors define the “meta-laws” governing host–pathogen co-stability. Entropy and information flow measures, derivable from the temporal series of B, Q, I and T , can quantify coherence between the interacting subsystems.

In summary, our theoretical experiment formalizes the mathematical structure through which lawful biological relations can be experimentally investigated. By aligning topological self-organization with physiological observables, it establishes a new route for quantifying the spontaneous emergence of order in host–pathogen systems such as *Streptococcus pyogenes*.

WHAT FOR? ADVANTAGES DERIVED FROM THE STREPTOCOCCUS PYOGENES IMPLEMENTATION OF THE AUTOGENETIC CHAMBER

The parameterized implementation of the *Autogenetic Chamber* for *Streptococcus pyogenes* (GAS) colonization provides not only a theoretical model of self-organizing lawfulness but also a range of quantifiable biomedical insights. The following paragraphs summarize the measurable biological, therapeutic and experimental advantages arising from this system.

Predictive differentiation between carriage, infection and eradication regimes. One major advantage lies in its ability to mathematically discriminate among the three major clinical states of *S. pyogenes* interaction with the human epithelium: asymptomatic carriage, acute infection and antibiotic-mediated clearance (Gera and McIver, 2013). This discrimination does not rely on fixed threshold definitions but arises naturally from feedback coupling between bacterial growth, quorum signaling, immune response and mucus clearance. The model identifies quantitative boundaries—specifically, $k_N \approx 0.45 \text{ h}^{-1}$ for immune killing and $\kappa_{\text{mcc}} \approx 0.76 \text{ h}^{-1}$ for mucociliary removal, beyond which infection collapses into eradication. These values can be used experimentally to design therapeutic protocols aiming not simply at bacterial death but at shifting the entire system toward the eradication attractor. Unlike empirical dose–response tables, this approach predicts the minimal host or drug intervention required to move the infection into a lawful self-stabilizing regime.

Quantitative assessment of immune efficiency and tolerance balance. The explicit coupling between quorum and immune variables enables a quantitative definition of “immune coherence,” measured as the mutual information $I(B;I)$ between bacterial density and immune activity. High $I(B;I)$ values (≥ 0.8 bits in normalized units) indicate effective immune surveillance, whereas lower values correspond to tolerance or latent carriage. The model predicts that asymptomatic carriers operate in a low-entropy regime with reduced but steady immune signaling (typically cytokine decay constants $\gamma_{\text{cyt}} = 0.2\text{--}0.3 \text{ h}^{-1}$) allowing bacterial persistence without overt inflammation. Clinically, this provides a framework for interpreting variable patient responses: rather than classifying them by absolute bacterial load, they can be characterized by their position along the $I(B;I)$ –entropy continuum. This insight can guide the design of immunomodulatory treatments enhancing information transfer rather than simply increasing immune strength, thereby restoring efficient host–pathogen synchronization without triggering excessive tissue damage.

Identification of optimal antibiotic timing and concentration windows. Incorporating pharmacodynamics directly into the chamber equations produces precise quantitative predictions for antibiotic efficacy as a function of time and dosage. Simulations indicate that for β -lactam antibiotics (penicillin G and amoxicillin), the product $T_{>\text{MIC}}$ must exceed approximately 40% of the exposure window to reach the eradication attractor. For instance, with $k_{\text{max}} = 2.0 \text{ h}^{-1}$, $h = 2$ and $\text{MIC} \approx 0.06 \mu\text{g mL}^{-1}$, the chamber predicts clearance at $\sim 9 \text{ h}$ for a $0.1 \mu\text{g mL}^{-1}$ dose maintained over 12 h. Below this range, oscillatory persistence occurs, corresponding to recurrent infection cycles. These predictive intervals could guide optimized dosing regimens—balancing efficacy with microbiome preservation, without reliance on population-averaged pharmacokinetic data. This method identifies how variations in mucosal clearance (κ_{mcc}) alter pharmacodynamic outcomes, implying that patients with reduced airway clearance may require proportionally higher local concentrations to achieve the same dynamical shift.

Mechanistic understanding of biofilm emergence and collapse. The quorum-driven feedback term $f_Q(Q) = 1/(1 + e^{-\sigma(Q-Q_c)})$ describes the sigmoidal transition between commensal and virulent phenotypes. Parameterization at $Q_c \approx 1 \text{ nM}$ predicts the onset of coordinated biofilm formation. Under low-clearance, low-immune conditions (e.g., $k_N < 0.1 \text{ h}^{-1}$, $\kappa_{\text{mcc}} < 0.05 \text{ h}^{-1}$), the model stabilizes biofilm-like steady states with $B \approx 0.8K$ and $Q > 1.1 \text{ nM}$. External perturbations such as immune activation or antibiotic influx can trigger collapse via bifurcation, a process analogous to sudden biofilm dispersal. This reproduces experimentally observed threshold-like responses and suggests that precise modulation of quorum parameters, rather than continuous antimicrobial pressure, can induce controlled disassembly of biofilms. From a therapeutic perspective, this implies that local quorum inhibitors or diffusivity modifiers could act synergistically with antibiotics to destabilize biofilm equilibria while minimizing host tissue stress.

Quantification of host mechanical and clearance contributions. Because mucus velocity enters the model through the advective term $\kappa_{\text{mcc}} = v_{\text{mcc}}/L$, physiological variability in clearance efficiency can be translated directly into measurable infection outcomes (Cobarrubia et al., 2021). For example, reducing v_{mcc} from 20 mm min^{-1} (healthy airway) to 2 mm min^{-1} (stagnant cryptic niche) decreases κ_{mcc} tenfold, shifting the equilibrium from clearance to persistence even under constant immune

killing. This parameter sensitivity highlights how anatomical microenvironments like tonsillar folds serve as structural attractors for chronic carriage. Clinically, it suggests that mechanical therapies enhancing mucus flow or modulating epithelial hydration could restore clearance regimes without antibiotics, providing a non-pharmacological adjunct in recurrent GAS pharyngitis. The model thus quantifies the contribution of purely mechanical parameters to infection dynamics, integrating biomechanics with microbiology.

Measurement of entropy production as a biomarker of infection state. Entropy production rate $\dot{S} = -\int (\partial_t p) \ln p \, dx$ serves as a scalar descriptor of system-level dissipation. In the parameterized chamber, acute infection corresponds to high entropy rates ($\dot{S} > 0.15 \, k_B \, \text{h}^{-1}$), while asymptomatic carriage stabilizes around $\dot{S} \approx 0.03 \, k_B \, \text{h}^{-1}$. Clearance reduces entropy production to near zero. These quantitative values can be experimentally approximated by tracking fluctuations in cytokine and bacterial concentration time series, allowing entropy to serve as a measurable biomarker of disease phase. This transforms a theoretical construct into a clinically useful diagnostic index, capable of distinguishing productive inflammation from stable tolerance without invasive sampling. Entropy-based classification may also enable personalized monitoring of treatment response through simple kinetic measurements.

Integrative predictive map of therapeutic interventions. By combining immune, antibiotic and mechanical parameters, the model constructs a three-dimensional therapeutic manifold where each axis, i.e., immune strength (k_N), clearance efficiency (κ_{mcc}) and drug exposure ($T > \text{MIC}$), defines a plane of potential recovery. The manifold reveals that moderate adjustments in any single axis can compensate for deficits in others, a principle of therapeutic equivalence within co-regulated systems. For instance, a 20% increase in κ_{mcc} can reduce antibiotic requirements by ~30% and a twofold increase in k_N can shorten necessary antibiotic exposure by 25%. This predictive relationship among physiological and pharmacological factors could stand for a practical quantitative tool for individualized treatment optimization, unifying heterogeneous patient data within a single geometrical representation.

Broader biological implications of the parameterized model. Beyond *S. pyogenes*, the chamber's parameterization framework can generalize to other mucosal pathogens such as *Haemophilus influenzae*, *Neisseria meningitidis* or commensal-pathogen hybrids like *Streptococcus pneumoniae*. The same recursive structure allows each species to be represented by its characteristic diffusion constants, quorum thresholds and immune response profiles. This enables comparative quantification of stability ranges, e.g., determining why *S. pyogenes* forms robust carriage states while *N. meningitidis* typically transitions more rapidly to clearance. Thus, our model might function as a cross-species platform for evaluating host-pathogen co-stability, with utility in vaccine development, microbiome engineering and drug screening pipelines.

In conclusion, the parameterized *Autogenetic Chamber* for *S. pyogenes* provides a fully quantifiable synthesis theoretically able to link molecular scale signaling, cellular immune kinetics, mechanical clearance and pharmacological action. By grounding all feedback processes in experimentally accessible parameters, it converts abstract self-organization into a tangible computational instrument for medical and biological research.

Conclusions

We formalized the *Autogenetic Chamber* as a theoretical framework capable of generating lawlike regularities from within self-organizing biological systems. The model, instantiated through the parameterized case of *Streptococcus pyogenes* colonization, demonstrated how measurable phenomena such as microbial growth, immune response and environmental transport can co-produce stable, lawful configurations without reliance on externally imposed rules. By embedding biological constants and empirical ranges directly into recursive coupling equations, the chamber revealed that the persistence, clearance or reactivation of infection correspond to stable attractor states emerging from feedback balance rather than fixed deterministic causes. This framework

thereby redefines the relation between law and behavior: the regularities traditionally viewed as explanatory precedents become emergent properties of interaction itself.

The *Autogenetic Chamber* provides a conceptual advance over existing models by establishing a unified formalism for dynamics, observation and constraint. Its novelty lies in transforming the observer from a passive external reference into an active component of the system, influencing and being influenced by the evolving configuration. This recursive closure between system and observation reintroduces internal necessity into biological description, suggesting that reproducibility and intelligibility are not epistemic accidents, but intrinsic consequences of self-consistent feedback. The framework's advantage resides in its mathematical economy: a single set of coupled relations accounts for both material and informational processes, eliminating the need to postulate external laws or empirical adjustment. Compared to traditional differential models or agent-based simulations, which fix parameters a priori, our chamber continuously recalibrates them as products of interaction, yielding an internally generated form of scientific lawfulness.

Systems biology treats laws as invariant templates governing interactions; the chamber instead views them as invariants arising from the recursive stability of those interactions. Statistical and network models describe correlations or causal paths, but rarely include the observer's role in shaping data; the chamber incorporates observation as a dynamic manifold that co-evolves with system states. Topological and information-theoretic methods capture global coherence but not its genesis; the chamber unites these aspects through feedback recursion, producing local-to-global transitions in which geometry, information and dynamics are inseparable (Zenil et al., 2016; Hernández-Lemus 2025; Varley et al., 2025). This synthesis enables quantification of law emergence without presupposing fixed reference points, showing that the very conditions for measurement and interpretation evolve along with the system itself.

Our framework is constrained by idealizations. The assumption of continuous feedback and smooth coupling simplifies biological heterogeneity and the absence of stochastic perturbations limits its applicability to noisy real-world systems. The chamber's recursive closure, while theoretically powerful, may require empirical approximations to maintain computational tractability. Biological systems also operate across multiple temporal and spatial scales that are only partially captured by the model's continuous representation. Furthermore, embedding observation as a variable introduces methodological complexity: empirical validation of a model that includes its own measurement apparatus requires careful operational definition.

Potential applications of the chamber framework extend beyond the specific case of *S. pyogenes*. It can be adapted to study host–pathogen dynamics, metabolic regulation or ecological feedback, wherever recursive coupling among interacting subsystems produces emergent invariants. Our theoretical structure suggests testable hypotheses: for instance, that measurable biological thresholds correspond to bifurcation boundaries in feedback stability; that phase transitions in infection or immunity reflect reorganizations of systemic invariants; and that entropy minima and information plateaus mark zones of emergent lawfulness. The result could pave the way for a new kind of integrative medicine that treats infection not merely as bacterial growth to be suppressed, but as a lawful dynamical system whose equilibrium can be shifted toward health by precisely calibrated interventions. Potential advantages include predictive stratification of infection states, measurable indices of immune efficiency and entropy, optimization of antibiotic schedules and integration of mechanical and immunological therapies into a unified theoretical framework. On a broader level, our framework could guide a methodological shift toward experiments designed not only to measure outcomes, but to examine how observation itself alters system behavior, converting empirical science into a recursive, self-organizing enterprise.

Summarizing, our *Autogenetic Chamber* shows that biological lawfulness can arise from the continuous interaction of processes, constraints and observation. Law is no longer an external descriptor, but a dynamic invariant emerging from within the system. By formalizing the conditions under which feedback produces sustained order, the chamber replaces the search for fixed laws with a science of generative regularities. Every measurable pattern in biology becomes simultaneously a

product and a manifestation of the recursive dynamics that constitute it. The *Autogenetic Chamber* reframes the scientific enterprise itself. It replaces detached observation with participatory co-evolution, deterministic causation with recursive generation and empirical regularity with endogenous lawfulness in which laws, observers and systems evolve together as parts of a single autogenetic continuum.

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References

1. Camara, Makhtar, Assane Dieng and Cheikh Saad Bouh Boye. "Antibiotic Susceptibility of *Streptococcus pyogenes* Isolated from Respiratory Tract Infections in Dakar, Senegal." *Microbiology Insights* 6 (October 29, 2013): 71–75. <https://doi.org/10.4137/MBI.S12996>
2. Cobarrubia, Antonio, Jarod Tall, Austin Crispin-Smith and Antoni Luque. 2021. "Empirical and Theoretical Analysis of Particle Diffusion in Mucus." *Frontiers in Physics* 9 (November 23): 594306. <https://doi.org/10.3389/fphy.2021.594306>
3. Costa Baciú, Dan. 2024. "Causal Modeling and Thermodynamics: Towards a New Convergence of the Two Fields." *BioSystems* 246 (December): 105338. <https://doi.org/10.1016/j.biosystems.2024.105338>
4. Dmitriev andrey V. and Olga A. Totolian. 2021. "Group A *Streptococcus* Rgg/SHP Quorum-Sensing System: Molecular Mechanisms and Physiological Functions." *Frontiers in Microbiology* 12: 637–49. <https://doi.org/10.3389/fmicb.2021.637049>
5. Fahy, John V. and Burton F. Dickey. 2010. "Airway Mucus Function and Dysfunction." *New England Journal of Medicine* 363 (23): 2233–47. <https://doi.org/10.1056/NEJMra0910061>
6. Gera, Kanika and Kevin S. McIver. 2013. "Laboratory Growth and Maintenance of *Streptococcus pyogenes* (The Group A *Streptococcus*, GAS)." *Current Protocols in Microbiology* 30 (October 2): 9D.2.1–9D.2.13. <https://doi.org/10.1002/9780471729259.mc09d02s30>
7. Haslwanter, Thomas. 2021. "Parameter Fitting." In *Hands-on Signal Analysis with Python*, 189–205. Cham: Springer. https://doi.org/10.1007/978-3-030-57903-6_8

8. Hernández-Lemus, Enrique. 2025. "Topological Data Analysis in Single Cell Biology." *Frontiers in Immunology* 16 (September 2): 1615278. <https://doi.org/10.3389/fimmu.2025.1615278>
9. Hill, David B., Brian Button, Michael Rubinstein and Richard C. Boucher. 2022. "Physiology and Pathophysiology of Human Airway Mucus." *Physiological Reviews* 102 (4): 1757–1836. <https://doi.org/10.1152/physrev.00004.2021>
10. Lock, Jaclyn Y., Taylor Carlson and Rebecca L. Carrier. 2017. "Mucus Models to Evaluate the Diffusion of Drugs and Particles." *Advanced Drug Delivery Reviews* 124 (November 5): 34–49. <https://doi.org/10.1016/j.addr.2017.11.001>
11. Pichichero, M. E., J. R. Casey, S. L. Block, R. Guttendorf, H. Flanner, D. Markowitz and S. Clausen. 2008. "Pharmacodynamic Analysis and Clinical Trial of Amoxicillin Sprinkle Administered Once Daily for 7 Days Compared to Penicillin V Potassium Administered Four Times Daily for 10 Days in the Treatment of Tonsillopharyngitis Due to *Streptococcus pyogenes* in Children." *Antimicrobial Agents and Chemotherapy* 52 (7): 2512–20. <https://doi.org/10.1128/AAC.00132-07>
12. Rahbari, Kate M., Jennifer C. Chang and Michael J. Federle. "A *Streptococcus* Quorum Sensing System Enables Suppression of Innate Immunity." *mBio* 12, no. 3 (May 4, 2021): e03400-20. <https://doi.org/10.1128/mBio.03400-20>. PMID: 33947757. PMCID: PMC8262891
13. Rikken, Gijb, Luca D. Meesters, Patrick A. M. Jansen, Diana Rodijk-Olthuis, Ivonne M. J. J. van Vlijmen-Willems, et al. 2023. "Novel Methodologies for Host–Microbe Interactions and Microbiome-Targeted Therapeutics in 3D Organotypic Skin Models." *Microbiome* 11, no. 1 (October 17): 227. <https://doi.org/10.1186/s40168-023-01668-x>
14. Scheuring, István, Jacob A. Rasmussen, Davide Bozzi, and Morten T. Limborg. 2022. "A Strategic Model of a Host–Microbe–Microbe System Reveals the Importance of a Joint Host–Microbe Immune Response to Combat Stress-Induced Gut Dysbiosis." *Frontiers in Microbiology* 13 (August 4): 912806. <https://doi.org/10.3389/fmicb.2022.912806>
15. Snäll, Johanna, Anna Linnér, Julia Uhlmann, Nikolai Siemens, Heike Ibold, Marton Janos, Adam Linder, Bernd Kreikemeyer, Heiko Herwald, Linda Johansson and Anna Norrby-Teglund. 2016. "Differential Neutrophil Responses to Bacterial Stimuli: Streptococcal Strains Are Potent Inducers of Heparin-Binding Protein and Resistin Release." *Scientific Reports* 6 (February 18): 21288. <https://doi.org/10.1038/srep21288>
16. Touré, Vasundra, Åsmund Flobak, Anna Niarakis, Steven Vercruysse, and Martin Kuiper. "The Status of Causality in Biological Databases: Data Resources and Data Retrieval Possibilities to Support Logical Modeling." *Briefings in Bioinformatics* 22, no. 4 (December 30, 2020): bbaa390. <https://doi.org/10.1093/bib/bbaa390>
17. Varley, Thomas F., Pedro A. M. Mediano, Alice Patania, and Josh Bongard. 2025. "The Topology of Synergy: Linking Topological and Information-Theoretic Approaches to Higher-Order Interactions in Complex Systems." *arXiv preprint arXiv:2504.10140 [cs.IT]*, April 14. <https://doi.org/10.48550/arXiv.2504.10140>
18. Watson, Michael E., Jr., Melody N. Neely and Michael G. Caparon. 2022. "Animal Models of *Streptococcus pyogenes* Infection." In *Streptococcus pyogenes: Basic Biology to Clinical Manifestations*, 2nd ed., edited by Joseph J. Ferretti and Dennis L. Stevens. Bethesda, MD: National Center for Biotechnology Information (US), National Library of Medicine. <https://www.ncbi.nlm.nih.gov/books/NBK586367/>
19. Zenil, Hector, Narsis A. Kiani, and Jesper Tegnér. 2016. "Methods of Information Theory and Algorithmic Complexity for Network Biology." *Seminars in Cell & Developmental Biology* 51 (March): 32–43. <https://doi.org/10.1016/j.semcdb.2016.01.011>

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