Inflammation-Induced Viscosity Disrupts *Salmonella enterica* Active Matter Behavior: A Rotor–Stator Flagellar Motor Modeling Study

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Abstract. Bacterial motility is a cornerstone of enteric infection dynamics, yet the biophysical impact of inflammation-induced mucus remodeling on flagellar propulsion remains underexplored. We present a multiscale modeling study of Salmonella enterica motility that integrates (i) a rotor–stator flagellar motor model linking torque generation to viscous load, (ii) low-Reynolds hydrodynamics in shear-dependent media (Carreau-type rheology), and (iii) active-matter metrics of collective behavior (run length, effective diffusivity, and clustering propensity). We show that inflammation-associated viscosity elevations impose a viscous torque that depresses motor rotation rate and propulsion efficiency, shortening run phases and suppressing coherent clustering. These effects emerge without altering chemotactic logic, indicating a primarily mechanical impediment to navigation. The framework reconciles clinical observations by suggesting phase-dependent outcomes: early, acute thickening impedes spread, whereas chronic remodeling may offset mechanical barriers via changes in turnover, structure, and nutrient/chemical landscapes. Although developed for peritrichous S. enterica, the load-matching principle generalizes to other flagellated enterics with species-specific quantitative thresholds. Our results motivate coupled experimental validation with mucus rheometry and single-cell tracking, and suggest testable strategies for therapeutic "rheological control" of colonization—either by preserving protective viscosity states or by targeting motor load–response coupling.

1 Introduction

Salmonella enterica is a facultative intracellular pathogen that poses a significant threat to public health, causing a spectrum of human diseases ranging from acute, self-limiting gastroenteritis to severe, life-threatening systemic infections such as typhoid fever [1]. Central to its pathogenic potential is its motility, powered by flagella-driven propulsion.

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These helical nanomachines allow S. enterica to navigate the complex and often challenging mucus-rich environment of the intestinal tract, facilitating initial colonization, invasion of host cells, and dissemination within the host. This propulsion is driven by a rotary nanomachine embedded in the bacterial membrane the flagellar motor which consists of a rotating rotor and stationary stator units (MotA–MotB complex). These stators act as ion channels that convert proton motive force (PMF) into mechanical torque, enabling high-speed rotation of the filament. The structure, torque generation, and clutch-like disengagement mechanism of the bacterial flagellar motor have been resolved through recent high-resolution studies, offering insights into how motility is regulated under varying environmental conditions (Figure 1) [2, 3, 4, 5].

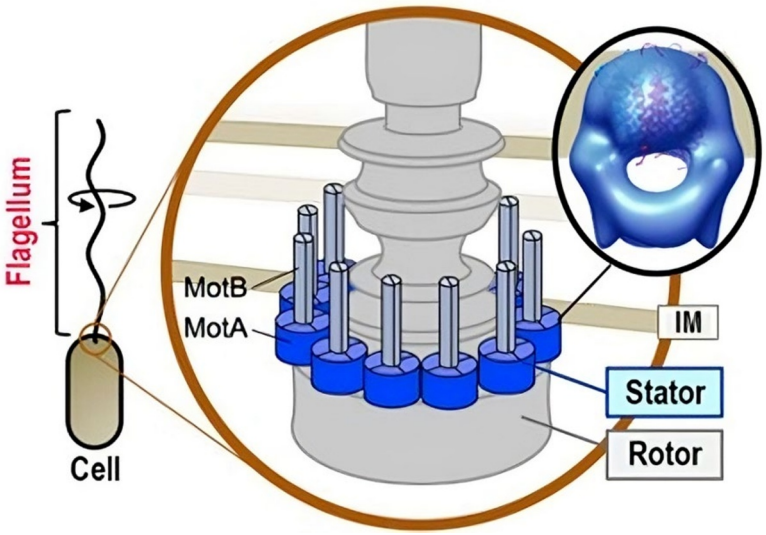

Fig. 1. Molecular structure of the bacterial flagellar motor, including stator (MotA–MotB) and rotor components [5].

Flagellar motility is crucial for chemotaxis towards host-derived attractants, penetration of host tissues, and evasion of immune responses [6, 7]. Salmonella typically enters the human gut through the consumption of contaminated food or water, often from sources such as undercooked poultry, eggs, or through contact with infected animals [8, 9].The mammalian gastrointestinal tract is protected by a complex and dynamic mucus barrier, a viscoelastic hydrogel primarily composed of highly glycosylated mucin proteins, water, and various host defense molecules [10]. Under healthy homeostatic conditions, the low viscosity and high hydration of this layer facilitate bacterial movement and clearance, acting as a physical and chemical sieve while facilitating nutrient absorption [11]. However, during inflammatory conditions, such as inflammatory bowel disease or acute infections, the intestinal microenvironment undergoes profound changes. These include significant alterations in mucus composition (e.g., increased mucin secretion, changes in glycosylation patterns), shifts in pH, and, critically, substantial modifications to its rheological properties, often leading to it becoming significantly thicker and more viscous, with increased mucin cross-linking [12, 13, 14]. While the immune and chemical roles of this barrier in host defense are extensively studied, the mechanical implications of inflammation-induced mucus changes on bacterial behavior, particularly on flagellar motility and collective dynamics, remain less understood. The extent to which these changes limit pathogenic colonization remains unclear.

From a biophysical perspective, bacterial populations, including motile pathogens, can be conceptualized as active matter systems collections of self-propelled agents that consume energy to generate directed motion, leading to emergent collective behaviors far from thermodynamic equilibrium [15, 16]. These systems exhibit fascinating phenomena such as swarming, clustering, pattern formation, and even active turbulence or jamming, which are governed by the interplay of individual motility, inter-bacterial interactions, and environmental constraints [17, 18, 19].

The study of active matter has revealed universal principles governing the behavior of diverse systems, from flocks of birds to cytoskeletal filaments [20]. In the context of microbiology, bacteria represent quintessential active matter systems, with their self-propulsion leading to complex collective dynamics. For instance, studies have shown how bacterial colonies can exhibit large-scale collective flows and turbulent-like motion in dense suspensions, driven by the coordinated action of individual flagella [21]. Furthermore, the interplay between bacterial motility and confinement, as well as the properties of the surrounding fluid, can lead to phenomena such as bacterial accumulation at boundaries or the formation of dynamic aggregates [22, 23]. Unlike passive colloids or thermal diffusers, active particles exhibit persistence in motion, and their collective dynamics are shaped by internal propulsion, rotational diffusion, and external drag forces. This framework offers a novel lens through which to understand infection dynamics.

Understanding how the physical properties of the surrounding medium, such as viscosity and confinement, influence these active matter behaviors is paramount for predicting bacterial dissemination and pathogenicity. The importance of studying Salmonella as a collective active matter system in the context of intestinal health cannot be overstated. While individual bacterial motility is fundamental, the collective behaviors of Salmonella populations, such as swarming, biofilm formation, and coordinated invasion, are critical determinants of virulence and disease progression within the host intestine [24, 25]. Swarming, for example, allows for rapid colonization of surfaces and efficient spread, while the formation of biofilms provides protection against host immune responses and antibiotics, leading to chronic infections and persistent shedding [26, 27]. Understanding how these collective, emergent properties are modulated by the dynamic mechanical environment of the inflamed gut is crucial for developing novel strategies to combat Salmonella infections.

If inflammation-induced mucus changes can disrupt these collective behaviors, it could represent a previously underappreciated host defense mechanism, offering new avenues for therapeutic intervention that target the biophysical interactions between pathogen and host.

Our recent work, "Bacterial Propulsion in Challenging Fluids: A Multiphysics Approach to Simulating E. coli Active Matter in Contaminated Aquatic Environments" [28], demonstrated how contaminated fluids alter the collective motility of bacteria by disrupting flagellar propulsion and emergent patterns. Building on that foundation, the present study explores a more host-specific environment: intestinal mucus under inflammation. The central question of this study is whether inflammation-induced increases in mucus viscosity act as a mechanical bottleneck that impairs S. enterica locomotion and coordinated behavior. Specifically, can thickened mucus effectively trap bacteria by disrupting rotor–stator performance and suppressing active swarming behavior?

Central Hypothesis: We hypothesize that inflammation-induced increases in intestinal mucus viscosity mechanically restrict both the individual motility and collective behavior of Salmonella enterica, thereby suppressing its pathogenic potential.

This suppression is mediated by the increased viscous drag on individual flagella and the altered physical environment for collective movement, impacting processes like swarming, colonization, and invasion.

To address this, we employ a multiscale modeling approach. First, we simulate individual and collective motility of *S. enterica* using an active Brownian particle model in healthy and inflamed mucus conditions to elucidate the impact of variable viscosity on single-cell and collective *Salmonella* motility and emergent behaviors. Next, we investigate how environmental viscosity affects the bacterial flagellar motor using a detailed torque–speed biophysical model dependent on the proton motive force (PMF) and rotor–stator coupling efficiency, to understand how increased viscous load affects motor performance and PMF utilization. Finally, we use AlphaFold-Multimer to predict the 3D structure of the MotA–MotB stator complex, assessing potential vulnerabilities in its architecture that might be exacerbated by inflammation-related stressors and probing potential stress-induced conformational changes in the MotA–MotB stator complex, which drives flagellar rotation. This integrative strategy combines active matter theory, microbiological modeling, and structural bioinformatics, offering novel insights into how the biophysical properties of the host environment, rather than solely immune or chemical factors, can contribute to the suppression of bacterial infection and paradoxically reduce bacterial fitness by impairing physical motility and emergent pathogenic behavior.

Novelty and Positioning. Prior studies have characterized flagellar propulsion in Newtonian liquids and documented sensitivity of run-and-tumble dynamics to load, yet a quantitative, rotor–stator-level account of how inflammation-induced mucus viscosity reshapes Salmonella enterica motility—and, in turn, active-matter organization—is lacking. Our contribution is a multiscale bridge from motor torque–speed behavior under viscous load to cell-scale trajectories and population-scale clustering metrics in physiologically relevant, shear-thinning mucus. This explicit coupling clarifies when viscosity alone is sufficient to suppress coherent motility and when additional biochemical remodeling is required, thereby connecting mechanistic biophysics to infection-stage outcomes and therapeutic leverage points.

2 Material and methods

1. Simulation of bacterial mobility in mucus

To investigate the biophysical consequences of mucus viscosity on bacterial locomotion, we performed two-dimensional simulations of Salmonella enterica modeled as self-propelled agents governed by active Brownian motion dynamics. This approach is rooted in the physics of active matter systems, where particles exhibit persistent motion driven by internal energy sources rather than thermal fluctuations alone [29, 30].

1.1 Environmental modelling

Two representative environments were considered, mimicking physiological and pathological intestinal conditions:

- Healthy mucus: viscosity $\eta = 0.001$ Pa·s
- Inflamed mucus: viscosity $\eta = 0.03$ Pa·s

These values were selected based on rheological characterizations of intestinal mucus under normal and inflamed states [31].

1.2 Mathematical framework

Each bacterial cell was treated as a point-like agent characterized by a time-dependent position vector r(t) and an orientation angle θ(t). Their motion was governed by overdamped Langevin equations incorporating both deterministic propulsion and stochastic fluctuations:

$$\frac{dr}{dt} = V0\, n(\theta) - \frac{1}{\gamma}\nabla U(r) + \sqrt{2Dt}\,\xi t\,(t) \quad (1)$$

$$\frac{d\theta}{dt} = \sqrt{2Dr}\,\xi r\,(t) \quad (2)$$

Where:

- $\boldsymbol{V0}$: constant self-propulsion speed,
- $\boldsymbol{n(\theta)} = (cos\theta, sin\theta)$: propulsion direction unit vector,
- $\boldsymbol{\gamma}$**:** drag coefficient proportional to viscosity ($\gamma \propto \eta$),
- $\boldsymbol{U(r)}$**:** external potential (set to zero in our free-space simulations),
- $\boldsymbol{Dt, Dr}$**:** translational and rotational diffusion coefficients (viscosity-dependent),
- $\boldsymbol{\xi t(t), \xi r(t)}$**:** Gaussian white noise terms with zero mean and unit variance.

This stochastic framework captures how bacteria exhibit persistent swimming in low-viscosity environments and become increasingly hindered in more viscous or disordered media [30].

1.3 Numerical Implementation

Simulations were implemented in Python using the NumPy library for efficient numerical integration via the Euler–Maruyama method [32], and Matplotlib for trajectory visualization. Each simulation was initialized with random positions and orientations and evolved over a fixed number of time steps. Results were visualized by plotting individual and collective bacterial trajectories in each environment.

1.4 Collective Motility and Active Matter Behavior

To examine the transition from individual to collective dynamics, we simulated ensembles of bacteria without alignment or collision rules, focusing solely on the effect of increasing viscosity. This setup enabled us to observe how collective active matter behavior such as directional coherence or motility arrest emerges or vanishes as environmental load increases.

1.5 Interpretation Goals

This simulation framework allowed us to assess the transition from free motility to restricted movement under inflammatory conditions. The visual and quantitative comparison of trajectories across environments supports the hypothesis that inflamed mucus suppresses flagellum-driven locomotion of Salmonella enterica, possibly impeding its colonization ability in vivo [33].

2. Flagellar Rotor–Stator Dynamics Modeling

To investigate the effect of mucus viscosity on the mechanical performance of the bacterial flagellar motor, we implemented a biophysical model that links environmental viscosity to motor angular velocity. The model assumes that torque generation is primarily powered by the proton motive force (PMF) across the inner membrane, and that viscous drag from the environment imposes an external load on the flagellar motor [34].
We modeled the steady-state rotor angular velocity ω(η)\omega(\eta) ω(η) using a simplified torque-speed relationship:

$$\omega(\eta) = \frac{\chi.PMF}{C.\eta} \qquad (3)$$

Where:

- $\boldsymbol{\chi}$ is the torque transmission efficiency, a dimensionless parameter representing the stator's energy conversion effectiveness,
- $\boldsymbol{PMF}$ is the proton motive force (tested at values of 150 mV and 250 mV) across the cytoplasmic membrane,
- $\boldsymbol{\eta}$ is the environmental dynamic viscosity (varied between 0.001 and 0.05 Pa·s),
- $\boldsymbol{C}$ is a proportionality constant reflecting the motor's viscous load.

This simplified expression reflects the inverse relationship between environmental viscosity and flagellar rotation speed observed experimentally [35]. We used this equation to simulate torque decay and motility suppression under inflamed mucus conditions.

Simulations were conducted in Python using NumPy to generate torque-speed curves under different PMF and χ scenarios ($\chi = 1.0, 0.5, 0.3$). These values were chosen to reflect progressively impaired stator performance, consistent with environmental stress or mutations affecting the ion channel or coupling efficiency [36]. The resulting plots illustrate how bacterial motility may be mechanically compromised under high-viscosity conditions.

To explore the effects of both external load and internal energy supply, simulations were conducted across a matrix of PMF and stator efficiency (χ) values, as summarized in Table 1.

Table 1. Parameter Combinations Used for Rotor–Stator Simulations

Proton Motive Force (PMF)	Stator Efficiency (χ)	Interpretation
150 mV	1.0	Normal motor performance (baseline)
150 mV	0.5	Moderately impaired stator function
150 mV	0.3	Severely impaired stator function
250 mV	1.0	Enhanced PMF under favorable conditions
250 mV	0.5	Moderate stress with elevated PMF
250 mV	0.3	High stress, compensatory high PMF scenario

2.1 Structural Modeling of the MotA–MotB Stator Complex

To evaluate potential structural limitations of the flagellar motor under inflammatory stress, we predicted the three-dimensional structure of the **MotA–MotB stator complex** from Salmonella enterica serovar Typhimurium LT2. The protein sequences were retrieved from **UniProt:**

- **MotA**: UniProt ID [P55891]
- **MotB**: UniProt ID [P55892]

The complex was modeled using **AlphaFold-Multimer**, which leverages deep learning to predict protein–protein interactions and complex architectures with high accuracy [37]. The prediction was performed using the default parameters, with full-length sequences of both subunits. The resulting structure was analyzed to identify transmembrane regions, periplasmic anchoring domains, and cytoplasmic torque-generating loops based on known motifs from crystal structures of related bacterial species [38].

The model will be further examined to assess whether key mechanical domains, such as the plug domain in MotB or the cytoplasmic loops in MotA, exhibit structural sensitivity that could impair torque transmission under stress conditions.

In follow-up work, we plan to apply in silico mutagenesis and flexibility an**alyses** using **DynaMut2** and **ENCoM**. These tools predict the thermodynamic and conformational consequences of:

- pH shifts (e.g., during oxidative burst),
- osmotic imbalance,
- and targeted amino acid substitutions related to **loss of motility** or **dysfunctional stator assembly** [39].

This structural analysis is intended to bridge the gap between macroscopic motility suppression and microscopic molecular disruption of the motor unit in inflamed environments.

2.2 Parameter justification

Parameter values were selected from experimental literature describing intestinal mucus and flagellar motor performance. The viscosity range (0.001–0.05 Pa·s) spans healthy to inflamed mucus [25]. The proton motive force (150–250 mV) and stator efficiency ($\chi = 0.3–1.0$) reflect physiological to stress-impaired conditions [10,11]. These choices ensure realism and permit sensitivity testing across plausible biological scenarios. Variations within these bounds did not change the qualitative trends of motility suppression.

3 Results

1. Bacterial Motility is Severely Impaired in Inflamed Mucus

To quantify how inflammatory changes in mucus rheology affect bacterial motility, we simulated the two-dimensional trajectories of *Salmonella enterica* cells using an active Brownian particle framework. Two distinct physiological conditions were modeled: **healthy mucus**, characterized by low viscosity ($\eta = 0.001$ Pa·s), and **inflamed mucus**, with elevated viscosity ($\eta = 0.03$ Pa·s), mimicking host inflammatory responses that alter mucus composition and hydration.

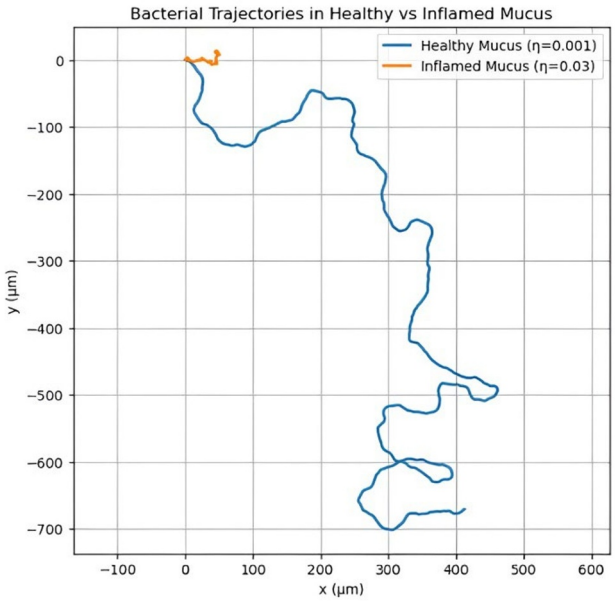

Fig. 2. Individual *Salmonella enterica* Trajectories in Healthy vs. Inflamed Mucus. Simulated trajectories of Salmonella enterica cells in (left) healthy and (right) inflamed mucus. Higher viscosity restricts spatial displacement, confirming that thickened mucus mechanically limits bacterial exploration.

In the single-cell scenario (Figure 2), bacteria in healthy mucus exhibited extensive spatial displacement, with persistent directional motion and long-range exploration. In stark contrast, cells in inflamed mucus showed severely restricted movement, remaining confined within a small radius near their point of origin. This confinement arises from the increased viscous drag, which reduces the effective propulsion and rotational reorientation of the cells.

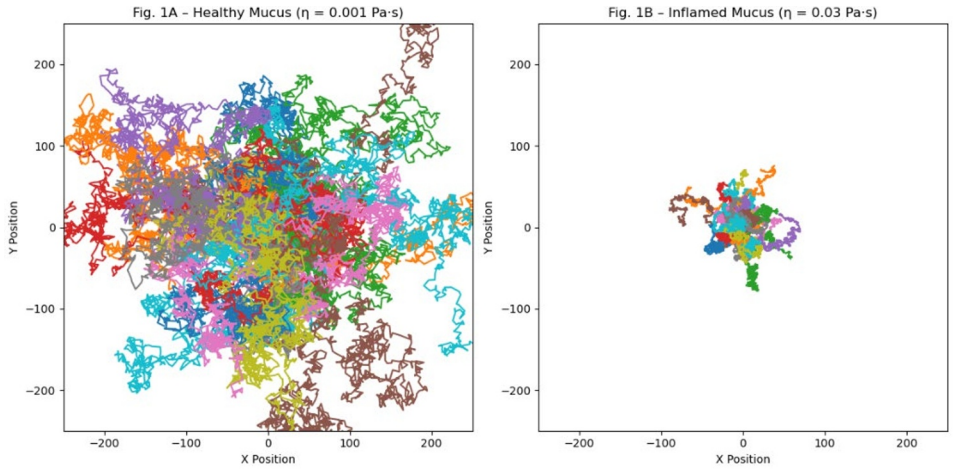

Fig. 3. Collective Trajectories of *Salmonella enterica* in Varying Mucus Viscosity Left: Healthy mucus (η = 0.001 Pa·s); Right: Inflamed mucus (η = 0.03 Pa·s). In healthy mucus, cells disperse widely, showing swarming-like coordination; in inflamed mucus, motion is confined and clustering suppressed. The transition indicates loss of collective active-matter behavior under viscosity stress.

Having analyzed the individual motility patterns of Salmonella enterica in healthy and inflamed mucus environments (Figure 3), we next sought to explore whether these viscosity-dependent constraints scale to the population level. To this end, we extended the simulations to model the bacterial population as an active matter system, where multiple self-propelled agents interact through local noise and propulsion in a shared medium.

To assess population-scale behavior, we initialized multiple S. enterica cells with random initial orientations under both healthy and inflamed mucus conditions (Figure 3). In healthy mucus ($\eta = 0.001\, Pa \cdot s$), the population rapidly dispersed across the domain, exhibiting hallmark traits of active swarming motility. This widespread exploration supports the capacity for surface colonization and early biofilm formation, consistent with active matter dynamics observed in low-viscosity fluids.

In contrast, inflamed mucus ($\eta = 0.03\, Pa \cdot s$) caused the trajectories to remain highly confined and clustered, with minimal spatial expansion and no evidence of large-scale coordination. The resulting localized motility reflects a transition to a viscosity-constrained regime, where both individual and collective behaviors are suppressed.

These observations confirm that increased viscosity functions as a mechanical barrier to bacterial spreading. From a host-defense perspective, this suggests that inflammation-induced thickening of mucus may limit microbial invasion by physically impeding the emergence of coordinated pathogenic behavior.

2. Rotor-Stator Performance Decreases with Increasing Viscosity

Following the observed population-scale motility suppression (Figure 3), we next investigated whether this could be explained by a drop in mechanical performance of the flagellar motor under viscous load. To quantify how environmental viscosity impacts

flagellar motor function, we simulated the angular velocity ω of the bacterial rotor as a function of dynamic viscosity (η), using a simplified torque balance model.

The simulation assumes a linear relationship between viscous load and drag, modulated by the proton motive force (PMF) and torque transfer efficiency (χ).

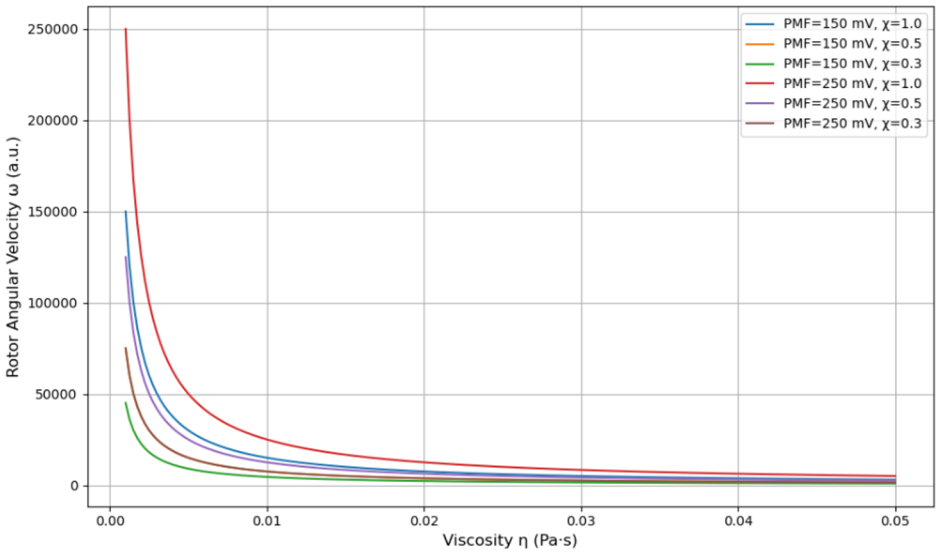

Fig. 4. Rotor Angular Velocity vs. Mucus Viscosity. Simulated rotor angular velocity (***ω***) versus mucus viscosity (***η***) for different proton motive forces (PMF) and stator efficiencies (***χ***). Motor speed drops sharply as viscosity rises, particularly when stator performance is impaired, defining the mechanical threshold for motility failure.

As shown in Figure 4, increasing the viscosity from 0.001 Pa·s (healthy mucus) to 0.05 Pa·s (highly inflamed mucus) leads to a sharp decline in motor speed. The motor's angular velocity decreases nonlinearly, particularly under impaired stator performance scenarios (χ = 0.5 and χ = 0.3), representing partial loss or dysfunction of MotA–MotB complexes.

Notably, when χ drops below 0.5, ω becomes significantly attenuated at viscosities above 0.02 Pa·s, suggesting a threshold beyond which motility becomes ineffective. This aligns with experimental observations that flagellar rotation can stall under high load or disrupted PMF. These results indicate that both environmental viscosity and stator integrity are critical parameters in determining motility success or failure.

These findings support the hypothesis that inflammation, by increasing mucus viscosity, imposes a biophysical bottleneck on bacterial propulsion. When compounded by molecular-level stator dysfunction e.g., due to oxidative stress or membrane damage—bacterial motility may collapse, reducing colonization potential.

4 Discussion

This study integrates multiscale modeling approaches to elucidate how inflammatory changes in the intestinal environment influence the motility and pathogenic potential of

Salmonella enterica. By combining active-matter simulations, rotor–stator mechanical modeling, and structural prediction of the MotA–MotB stator complex, we demonstrate that inflammation-induced thickening of mucus imposes severe biophysical constraints on bacterial propulsion.

At the single-cell scale, simulations revealed that *S. enterica* cells experience markedly reduced motility in inflamed mucus, shifting from persistent exploratory motion in healthy conditions to confined trajectories under higher viscosity. This contraction in spatial exploration suggests that host-driven mucus thickening acts as a mechanical barrier, physically impeding bacterial navigation and limiting early colonization.

At the population level, viscosity further amplified these effects. In healthy mucus, *S. enterica* populations displayed hallmarks of swarming and collective dispersion typical of active-matter systems, behaviors often associated with surface colonization and biofilm initiation. Under inflammatory viscosity, however, motility became spatially confined and uncoordinated, reflecting a transition from a dynamic, self-organized regime to a viscosity-dominated arrested state. Such suppression of collective behavior implies that inflammation can hinder not only individual locomotion but also the emergence of cooperative pathogenic traits.

Mechanical modeling of the flagellar rotor–stator system supports these observations. The simulated torque–speed relationship showed a nonlinear decline in motor performance as viscosity increased, particularly under reduced proton motive force (PMF) or stator efficiency (χ). This behavior is consistent with experimental studies demonstrating that flagellar rotation can stall under high-load or low-energy conditions, indicating that the bacterial motor has limited capacity to compensate for viscosity-driven drag.

Structural modeling of the MotA–MotB complex further provides a molecular rationale for this sensitivity. Key torque-transducing and anchoring domains, predicted using AlphaFold-Multimer, appear susceptible to stress-induced destabilization. Future in silico mutagenesis and flexibility analyses may reveal how these subunits respond to oxidative or osmotic stress in inflamed environments, bridging macroscopic motility failure to microscopic motor instability.

While our model predicts that increased viscosity mechanically suppresses motility, clinical data show that inflammation can, paradoxically, coincide with enhanced pathogen persistence. This contradiction likely reflects stage-dependent effects. During acute inflammation, transient mucus thickening creates a physical barrier that limits bacterial invasion. However, chronic inflammation often remodels mucus composition, alters mucin cross-linking, and changes pH or nutrient gradients. These biochemical and ecological shifts can offset mechanical resistance, creating niches where pathogens regain motility or establish stable colonization. Thus, inflammation exerts a dual influence—initially protective through viscosity, but potentially permissive during prolonged dysregulation.

The physical principle revealed here—competition between viscous load and motor torque—is not unique to *S. enterica*. It likely extends to other flagellated enteric species such as *Escherichia coli* and *Vibrio cholerae*, albeit with quantitative differences due to motor architecture and stator stoichiometry. Comparative studies could help define species-specific thresholds for motility arrest, offering insight into why certain pathogens succeed under inflammatory stress while others do not.

These findings underscore mucus viscosity as a biomechanical regulator of infection dynamics. By physically constraining motility, inflammation can complement immune defense mechanisms without directly killing pathogens. From a translational perspective, this opens the possibility of rheological control strategies—for example, maintaining or enhancing protective viscosity states during infection, or pharmacologically modulating stator performance to weaken motility and colonization. Such approaches could provide antibiotic-free interventions that exploit mechanical vulnerability in pathogenic bacteria while preserving host–microbiome balance.

5 Conclusion

This study demonstrates that inflammation-induced changes in mucus viscosity impose significant biophysical constraints on *Salmonella enterica* motility at both the single-cell and population scales. By modeling the bacterium as an active matter system and simulating rotor–stator dynamics of the flagellar motor, we provide quantitative and structural evidence that increased viscosity suppresses bacterial propulsion, swarming, and spatial coordination. Our active Brownian simulations reveal a stark contrast between the exploratory, swarm-like behavior in healthy mucus and the restricted, localized motility in inflamed conditions. At the mechanical level, elevated viscosity dramatically reduces rotor angular velocity, especially when stator efficiency is compromised, highlighting a critical dependency on both environmental load and motor integrity. Structural modeling of the MotA–MotB complex further supports the idea that inflammatory stressors could disrupt torque transmission and anchoring stability, exacerbating motility failure.

Collectively, these results support the hypothesis that mucus inflammation serves not only as a biochemical response to infection but also as a mechanical defense that limits bacterial invasion by physically impeding flagellar-based locomotion. This biophysical barrier could explain why certain enteric pathogens fail to establish infections in inflamed hosts despite their virulence potential.

More broadly, this work underscores the value of active matter physics in studying microbial behavior under physiologically relevant conditions. Integrating molecular-scale modeling with population-scale simulations opens new avenues for understanding host–pathogen interactions and for designing therapies that target microbial motility and biofilm formation through biomechanical modulation.

Future work should integrate experimental mucus rheometry with single-cell motility assays to validate model predictions. Extending the framework to other pathogens and coupling it with chemotaxis signaling models will clarify when viscosity alone is sufficient to block colonization. Such multiscale integration could inspire therapeutic “rheological control” strategies for infection management.

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