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COS700 Research Report

Agent-Based Modeling of Chemotaxis in Competitive Heterogeneous Environments

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October 2025

Abstract

Microbial communities represent highly complex, adaptable systems where collective behaviors of individual cells, largely driven by chemotaxis (the ability to sense and react to chemical gradients), determine population dynamics and spatial structure. Predicting the macroscopic outcomes of these microscopic interactions remains a challenging task, particularly when considering heterogeneous environments and competitive dynamics. Top-down mathematical models often overlook the critical impact of individual agent heterogeneity. To address this, this research implemented a generalized Agent-Based Model (ABM) in NetLogo, utilizing a modular and extensible framework to simulate chemotaxis within competitive, heterogeneous, and varied environments. This research bridges the gap between models focused narrowly on a single species or phenomenon and those striving for simulation realism within complex spaces. The model successfully integrates individual agent properties, a dynamic chemical environment, and physical obstacles, allowing individual decisions to generate system-wide emergent behaviors. The framework was validated against key biological phenomena derived from biological literature, including the logistic growth curve of a population, chemotactic swarming patterns, and the principle of competitive exclusion. The successful simulation of a realistic case in a complex wound bed environment further demonstrates the model's robustness and utility as a flexible platform for exploring complex issues in microbial ecology, with tangible applications in fields like bioremediation and therapeutic design.

Keywords:

Agent-Based Model, Bacterial Chemotaxis, Computational Biology, NetLogo, Multi-Agent Simulation, Microbial Ecology, Systems Biology.

Glossary of Terms

Aerobic An organism or process that requires oxygen to live or function.

Agent-Based Model (ABM) A computational model that simulates the actions and interactions of autonomous agents (like individual bacteria) to observe emergent behaviors in the system as a whole.

Antibiotic A substance, like Polymyxin B, that kills bacteria or inhibits their growth.

Biofilm A complex, structured community of microorganisms that adhere to a surface and are encased in a self-produced slimy matrix, offering protection and enhanced survival.

Bioremediation The use of microorganisms (like bacteria) to consume and break down environmental pollutants, cleaning up a contaminated site.

Chemotaxis The directed movement of an organism or cell in response to a chemical gradient (i.e., moving toward nutrients or away from toxins).

Competitive Exclusion An ecological principle stating that two species competing for the exact same limited resources cannot coexist at constant population values; one will eventually eliminate the other.

Facultative Refers to an organism that can switch between different metabolic pathways, such as using oxygen when it's present (aerobic) or using other methods when it's absent (anaerobic).

Flagella Whip-like appendages on bacteria that rotate to propel the cell, enabling movement.

Gram-negative A class of bacteria characterized by a thin cell wall and an additional outer membrane, which makes them resistant to certain antibiotics.

Gram-positive A class of bacteria characterized by a thick cell wall and no outer membrane.

Heterogeneous Environment An environment characterized by variability in spatial structure, chemical concentrations, or resource availability, often including obstacles.

Homogeneous Environment An environment lacking significant spatial variation in conditions or resources.

Hypoxic An environment that is deficient in oxygen.

Logistic Growth Curve A common "S-shaped" (sigmoidal) curve that models population growth in a resource-limited environment, showing an initial exponential phase followed by a leveling-off as resources become scarce.

Metabolism The set of chemical reactions within a cell that convert nutrients into energy, allowing the cell to move, grow, and reproduce.

Microbial Ecology The study of microorganisms in their natural environments and their interactions with each other and their surroundings.

Pathogen A microorganism, such as a bacterium or virus, that can cause disease.

Peptidoglycan A polymer forming the cell wall of bacteria. The thickness of this layer is the key difference detected by the Gram stain.

pH A measure of the acidity or alkalinity of a solution, on a scale typically from 0 (most acidic) to 14 (most alkaline), with 7 being neutral. Bacterial growth and activity are often sensitive to pH levels.

Planktonic The state of bacteria existing as free-floating or swimming individual cells, as opposed to being part of a stationary biofilm.

Pollutant Biodegradation The breakdown of harmful environmental pollutants by biological organisms, primarily microorganisms like bacteria.

Quorum Sensing A system of chemical communication bacteria use to monitor their population density. When density is high, they coordinate gene expression, often to trigger collective behaviors like biofilm formation or toxin production (e.g., using Autoinducer-2).

Run-and-Tumble The characteristic movement pattern of many bacteria, consisting of a straight "run" (flagella rotating together) followed by a random "tumble" (flagella rotating apart) to change direction.

1 Introduction

Microbial communities are among the most complex and adaptable systems on our planet. They have an incredible ability to establish and survive in a vast range of environments and circumstances due to individual and group behaviours. Chemotaxis is a significant driving force of these behaviors. Chemotaxis is the ability of bacteria to sense and react to chemical gradients in their environment [1]. This ability allows bacteria to forage for nutrients, flee from toxins, and organize group motion. The ability to model and easily experiment with this phenomenon is critical for the use of chemotaxis fields such as environmental bioremediation, designing novel antimicrobial therapy, and developing drug delivery systems with targeted action [2].

Predicting the macroscopic results of these microscopic interactions remains a daunting task. Population dynamics, spatial structure, and community stability are emergent properties that occur due to local interactions of heterogeneous individuals[3]. Top-down mathematical modeling overlooks the impact of these individual agents. This is where agent-based Modeling (ABM) comes into play. ABM is a bottom-up approach where rules are implemented at an agent level, resulting in emergent behaviours and patterns at the population level[4, 5].

Previous models have been implemented to simulate bacterial behaviours, but they are often focused on a single microbial species or a specific phenomenon or interaction. This research implements a generalized ABM in NetLogo with a modular and extensible framework to simulate chemotaxis in competitive, heterogeneous, and varied environments. The model is validated against key biological occurrences documented in

literature, comparing simulation outputs to expected qualitative patterns and quantitative growth dynamics, while using empirically derived data to drive the simulation. The model aims to bridge the gap between models focused narrowly on a single species or phenomenon and those striving for simulation realism within complex spaces.

2 Background

2.1 Mechanisms of Bacterial Chemotaxis

Some bacteria have appendages named flagella that enable them to move. This happens in a *run-and-tumble* pattern. This is done by the flagella being rotated counterclockwise to initiate a straight run and then clockwise to initiate a tumble to adjust the direction [6]. The ability of bacteria to sense the chemical gradients allows the bacteria to move in a more optimally devised directions rather than doing a random walk. This leads to bacteria moving together with a goal rather than spreading randomly. It has been found that this results in bacteria populations spreading faster and in turn growing faster due to more nutrients being found over a greater area [7]. It has also been observed that the highest concentration is found on the edge of the colony rather than the center when chemotaxis acts on the population. Even though the source of the gradient that attracts the bacteria may have little to no nutritional value, an increase in growth was still observed in them compared to bacteria with a lack of chemotactic sensing [8].

The sensing of these gradients does not come without cost, though, as the creation of the needed proteins and the act itself requires energy, just like the movement done during chemotaxis. This means that the energy expended by sensing and moving needs to be justified by the nutrients obtained. Chemotaxis also helps bacteria to avoid toxic and detrimental sources, as it guides the bacteria away from the source instead of staying near it and being affected negatively.

2.2 Applications of Chemotaxis

Due to bacteria being everywhere and chemotaxis being such a prevalent behavior of them, it is important to investigate how this ability can be applied to improve fields like medicine and conservation. Fiaz Ahmad et al. investigated this opportunity by looking at how polycyclic aromatic hydrocarbon-contaminated soils can be bioremediated by exploiting the sensory capabilities of various bacteria to seek out the pollutants and biodegrade them[9]. The study concluded that this is still a vaguely understood topic in light of how it can effectively be used in the real world.

Jonas Cremer et al. showed that the range expansion effect of chemotaxis enhances bacterial seeding for ecosystem recovery of soil[8]. Qi Xu et al. follow the same line of thinking as they sought out ways to apply chemotactic intelligence. They dived deeper into how chemotaxis can be used to create targeted drug delivery systems and improve disease control in an environment. Targeted drug delivery was further pioneered by Mohammed Almijalli et al. in 2021, with their research focusing on using a chemotaxis model to investigate the targeted delivery of drugs in nonlinear diffusion environments[10]. This

paper takes in account many real-world parameters of cells, like growth and wall elasticity, to create a very accurate model. It further demonstrates how valuable the field of the practical application of chemotaxis is. Using a simulation model like an ABM for this type of research might be more beneficial, as it takes individual cells more into account.

2.3 Gram Stain Classification

The Gram stain classification classifies bacteria into one of two groups, Gram-positive or Gram-negative, based on their cell wall structure. Gram-positive bacteria have thick, multi-layered peptidoglycan cell walls, where Gram-negative bacteria have a thinner peptidoglycan layer, which is surrounded by an additional outer membrane[11]. Due to the different wall structures, the two bacterial classes are susceptible to different types of toxins. For instance, Polymyxin B is an antibiotic that specifically targets the outer membrane of Gram-negative bacteria, thus being ineffective against Gram-positive species [12].

2.4 Energy Metabolism

Bacteria are classified into types based on their ability to produce energy in the presence as well as the absence of oxygen. Aerobic bacteria, such as *Pseudomonas aeruginosa*, are obligate aerobes, meaning they strictly require oxygen for cellular respiration to produce energy. In contrast, facultative organisms, like *E. coli* and *Salmonella enterica*, are metabolically flexible [11]. The type of respiration directly affects a species' performance in an environment.

2.5 Selection of Bacterial Species for Modeling

Bacterial species differ in how they perform and react in their environments; thus, it is important to select species that provide meaningful insight into the capabilities of the model.

Table 1: Bacterial Species

Species	**Speed (μm/s)**	**Run/Tumble Duration (s)**	**Preferred Attractants**
Vibrio cholerae	40-60	1.0-2.0 / 0.3-0.5	Aspartate, Autoinducer-2
Bacillus subtilis	15-25	0.3-0.8 / 0.1-0.3	Aspartate, Glucose, Autoinducer-2
Escherichia coli	20-30	0.5-1.0 / 0.1-0.2	Glucose, Aspartate, Autoinducer-2
Pseudomonas aeruginosa	25-40	0.8-1.5 / 0.2-0.4	Aspartate
Salmonella enterica	25-35	0.6-1.2 / 0.2-0.4	Glucose, Aspartate
Paenibacillus polymyxa	10-20	0.4-0.9 / 0.1-0.3	Glucose
Burkholderia cenocepacia	30-50	0.7-1.3 / 0.2-0.4	Aspartate, Glucose, Autoinducer-2

Table 2: Only attractants related to implemented chemicals are represented

Table 3: Bacterial Species

Species	**Repelled By**	**Energy Source**	**Taxis Sensitivity (μm)**	**Lifespan / Division Rate (min)**
Vibrio cholerae	None	Facultative	1-20	15-25 / 15
Bacillus subtilis	Butanol, Phenol	Aerobic	10-100	40-80 / 25
Escherichia coli	Phenol, Butanol	Aerobic	1-10	20-30 / 20
Pseudomonas aeruginosa	Phenols, NO	Aerobic	5-50	30-60 / 30
Salmonella enterica	None	Facultative	5-50	20-40 / 20
Paenibacillus polymyxa	None	Facultative	10-100	50-100 / 30
Burkholderia cenocepacia	Polymyxin B, Phenol, Butanol	Aerobic	20-120	60-120 / 40

Table 4: Only repellents related to implemented chemicals are represented

Table 5: Bacterial Species Selection (Ecological and Structural Parameters)

Species	**Stress Tolerance**	**Gram Stain**	**Size (μm)**	**Produced Chemicals**	**Preferred pH**
Vibrio cholerae	Moderate	Negative	3.0	Autoinducer-2	8.5
Bacillus subtilis	Extreme	Positive	7.0	Autoinducer-2	7.2
Escherichia coli	Moderate	Negative	2.0	Autoinducer-2	7.0
Pseudomonas aeruginosa	High	Negative	2.2	-	7.0
Salmonella enterica	High	Negative	3.5	Autoinducer-2	7.2
Paenibacillus polymyxa	High	Positive	5.0	Polymyxin B	7.0
Burkholderia cenocepacia	Extreme	Negative	3.0	-	6.8

Note: Data in tables 2, 4 and 5 are compiled and supported by a range of sources including [6, 13, 14, 15, 16, 17, 18, 19, 12, 20, 21, 22, 23, 24].

Escherichia coli is a benchmark bacteria species for chemotaxis functionality. It is one of the most extensively characterized biological systems [1, 6]. Being so well researched makes it a *E. coli* a prime canditate for validation purposes.

Species such as ***Vibrio cholerae*** and ***Pseudomonas aeruginosa*** are two other well researched bacterial species while being pathogenic in nature. *P. aeruginosa* is an opportunistic pathogen, where chemotaxis is integral to its ability to form resilient biofilms and colonize wounds [23]. Similarly, *V. cholerae* exhibits chemotaxis toward host-derived signals like serine, a key mechanism in host-pathogen interactions that could be a target for therapeutic intervention [14]. Thus *P. aeruginosa* and *V. cholerae* are good candiates for pathogenic experiments.

Bacillus subtilis and ***Paenibacillus polymyxa*** are usefull species in conservation and bioremediation applications. *B. subtilis* is particularly adapted to terrestrial environments, showing strong attraction to compounds common in soil [15]. *P. polymyxa* introduces a competitive dynamic, with its ability to produce antibiotic **Polymyxin B** [12]. Polymyxin B is a potent repellent as well as a defense mechanism. Furthermore, the inclusion of the extremophile ***Burkholderia cenocepacia***, known for its high resistance to antibiotics and environmental stressors, allows for investigation of more tolerant

bacteria.[19]. *B. cenocepacia*'s ability to sense Polymyxin B allows for testing the competitive natures of species.

2.5.1 Chemicals as Chemoeffectors in the Model

The chemical landscape in any environment is defined by a diverse set of chemoeffectors, substances that act as attractants, repellents, or signals. These compounds contribute differently to the gradients that guide bacterial navigation.

Table 6: Chemical Effectors

Chemical	**Type**	**Diffusion Rate ($\mu m^2/s$)**	**Effective Range (μM)**
Glucose	Attractant	800-1000	500-1000
Aspartate	Attractant	600-800	300-600
Phenol	Repellent	400-600	200-400
Butanol	Repellent	500-700	300-500
Autoinducer-2	Quorum signal	300-500	0.01-0.1
Polymyxin B	Repellent	200-400	0.1-1

Table 7: Chemical Effectors

Chemical	**Biological Role**	**Source**	**Metabolizable**
Glucose	Nutrient	Environment	Yes
Aspartate	Amino acid	Host/Environment	Yes
Phenol	Toxin	Environment	No
Butanol	Solvent stress	Environment	No
Autoinducer-2	Cell communication	Bacterial	No
Polymyxin B	Antibiotic	Bacterial	No

Note: Data in tables 6 and 7 are compiled and supported by a range of sources including [25, 26, 20, 27, 28, 29].

Attractants are chemicals signaling resource-rich zones, usually metabolizable as well. **Amino acids**, such as **aspartate**, and **sugars** like **glucose** are among the most potent chemoattractants for a wide range of bacteria species [1, 26]. The ability to efficiently sense and locate these compounds promotes bacterial foraging behavior.

Repellents on the other hand, signal environmental threats. Compounds like **phenol** and **butanol** are toxins that impair cellular integrity by disrupting membranes. Antibiotics, such as **Polymyxin B** create repellent gradients that influence bacterial distribution [28].

Quorum Sensing Molecules represent a unique class of chemoeffectors, such as **Autoinducer-2 (AI-2)**. Unlike metabolizable compounds like glucose, AI-2 functions purely as an information-carrying signal. The signalling allows bacteria to communicate and coordinate collective behaviors like biofilm formation [27]. Its presence adds a layer of social complexity to chemotactic navigation.

2.5.2 Environmental Contexts

Simulating bacterial chemotaxis in a variety of environmental scenarios is important for understanding how external conditions impact behavior. Each environment is characterized by unique parameters that shape bacterial motility and performance capabilities.

Table 8: Environmental Contexts

Environment	pH	Oxygen Level	Viscosity	Nutrient Availability
Lab Agar Plate	7.2	Aerobic	High	Abundant
Soil Microcosm	7.0	Aerobic	High	Scarce
Wound Site	7.4	Hypoxic	Moderate	Moderate
Lake Water	8.0	Variable	Low	Moderate

Note: Data in tables 8 are compiled and supported by a range of sources including [11, 30, **?**, 31, 32, 33].

Environmental factors such as pH and oxygen levels have vast effects on bacterial species and their abilities to perform. A **wound site**, for example, is often hypoxic and may have steep pH gradients, thus making it difficult for aerobic bacteria with a specific pH range to flourish[16]. Further environments like **lab agar plates**, with their high viscosity, present yet another challenge, favoring swarming motility over individual swimming [15]. Nutrient abundance that is dispersed throughout an environment also affects how easily bacterial populations can increase, leading to complex competitions based on sensing ranges and moving speeds of bacterial species.

2.5.3 Physical Obstacles and Spatial Constraints

Real-world environments are not empty spaces but rather heterogeneous environments containing physical obstacles that constrain bacterial movement and alter chemical landscapes. Incorporating spatial complexity is crucial for creating realistic simulations [34].

Table 9: Obstacle Types

Obstacle	Size (μm)	Permeability	Toxicity
Agar Wall	1000	Low	None
Polystyrene Bead	10-50	High	None
Necrotic Tissue	200-500	Moderate	Yes
Oil Droplet	50-200	None	Yes
Metal Oxide NP	0.1-1.0	None	Yes

Note: Data in this table are compiled and supported by a range of sources, including [35, 36].

Obstacles directly impact the chemotactic abilities of bacteria. When an object is encountered, it must first avoid the obstacle before the bacterium can act on the chemotactic signal again, thus forcing the bacterium on a detour. Furthermore, obstacles distort chemical gradient fields. An impermeable object, like an oil droplet or a metal nanoparticle [35, 36], will create a chemical "shadow", disrupting the smooth gradients that bacteria use to navigate. This can lead to navigational errors, as the local gradient may point in a direction that deviates from the overall source of the attractant.

2.6 Computational Approaches to Modeling Chemotaxis

There have been a few approaches to model chemotaxis. Multi-agent models were developed to explore chemotaxis in heterogeneous environments[34]. This was an important step as most earlier models used a homogeneous environment, which is not a close representation of the real world. This research was very helpful in understanding how the colonies would react to physical and chemical barriers, but still lacked the effect that other bacterial competitors would have. This is important to understand as competition is always present in real-world heterogeneous environments. This competition has not gone uninvestigated, as Congjian Ni built an ABM simulating how a bacterial population interacts and adapts when they are in competition with another species that produces a toxin that inhibits the other species [37]. They compared how the affected species respond and survive based on their movement and chemotactic efficiency. Thus, combining these two concepts, we can create a model that simulates the bacteria much more accurately.

Yuhai Tu created a quantitative model to represent and compute the dynamic signaling and detection of the bacteria in chemotaxis based on the environment and gradients they find themselves in [38]. Yung Tu provided a model to compare other models to and improved predictions. Quantitative models are very computationally expensive and struggle to model individuals in the greater population; this is where ABM efficiency lends itself to help. Emily G.Sweeney also created an ABM to model biofilm formation due to chemotactic behaviors[39]. This research is important as biofilm formation greatly increases the bacterial population's survivability. Thus, being able to simulate how chemotaxis impacts biofilms is important to understand and can be used in the

pharmaceutical field. The model they used simulated a 3D environment, as biofilms are not a 2D structure. This is noteworthy, as the real world operates in three dimensions, the choice of a 2D versus 3D model environment can potentially impact the accuracy and interpretation of simulation results, particularly for phenomena like biofilm formation.

2.7 Agent-Based Modeling and the NetLogo Platform

Agent-based modeling (ABM) is a powerful approach to simulating complex, spatially explicit dynamics of biological populations. The strength of an ABM's realism lies in the simulation of and decision-making of each individual agent. This differs from traditional equation-based models that use a top-down perspective to describe population-level behaviors [3]. The bottom-up approach allows for population-level behaviors and patterns to emerge from the collective actions of each independent agent acting upon its programmed rules[40]. This approach is exceptionally well-suited for systems where the heterogeneity of individuals and their local interactions are critical drivers of population-level behavior, such as in microbiology, ecology, and social science [5].

The NetLogo Environment: Architecture and Capabilities **NetLogo** is a multi-agent programmable modeling environment, perfectly suitable for the implementation of ABMs [41]. Developed at Northwestern University, it is designed to be an easy-to-use to use platform for novice modelers while still providing powerful tools for professional researchers [42]. Its architecture is built upon three core components:

- **Agents (Turtles):** Mobile agents within the simulation. In the current research context, a turtle could represent a bacterial cell. Each agent possesses individual properties such as its position, heading, and defined custom variables (`turtles-own`), allowing each agent to own unique attributes like age, energy level, or species. This inherent structure is ideal for capturing population heterogeneity in a simple and effective manner [40].

- **Environment (Patches):** The environment is a grid of static agents called patches. `Patches-own` allows custom variables to be assigned to patches, making them perfect for modeling spatially heterogeneous landscapes. This capability is fundamental for simulating environmental factors like resource concentration or chemical gradients. NetLogo includes powerful built-in primitives like `diffuse`, which calculates the diffusion of a chemical variable between patches over time, making it useful for modeling the formation and decay of chemical gradients in an easy, computationally effective manner[40].

- **Relationships (Links):** A link is a connection between two turtles, allowing for network modeling. These can represent social ties, physical connections, or genetic relationships, enabling the study of phenomena where network structure is a key component [40].

NetLogo as a Tool for Scientific Inquiry Beyond its architecture, NetLogo incorporates features that establish it as a robust platform for scientific research:

- **Integrated Visualization:** The NetLogo interface has real-time, graphical feedback on the simulation's state. The immediate visualization allows for good intu-

ition for implementation logic, debugging based on observation, and generating new hypotheses based on emergent patterns [42].

- **BehaviorSpace Experimentation Tool:** This feature is an automated tool that allows performing large-scale computational experiments. This is done by systematically sweeping through parameter spaces and *running* multiple replications, which is essential for sensitivity analysis and robust data collection [40].
- **Extensibility and Interoperability:** NetLogo's functionality can be extended through libraries as well as third-party programs like Python or R.

3 Problem Statement

Predicting the macroscopic results of these microscopic interactions remains a daunting task. Population dynamics, spatial structure, and community stability are emergent properties that occur due to local interactions of heterogeneous individuals[3]. Top-down mathematical modeling overlooks the impact of these individual agents. This is where agent-based Modeling (ABM) comes into play. ABM is a bottom-up approach where rules are implemented at an agent level, resulting in emergent behaviours and patterns at the population level[4, 5]. Many models have been implemented to simulate bacterial behaviours, but they are often focused on a single microbial species or a specific phenomenon or interaction [43, 44, 37, 7]. It is important to have a generalized, modular, and extensible model to enable experimentation in pharmaceutical and conservation fields [3, 4, 45]. Such a model is needed so that researchers with limited model-building skills are not prohibited from doing their research [46, 5, 40].

4 Related Work

4.1 Foundational Agent-Based Models of Chemotaxis

Early individual-based models have successfully replicated the biased random walk (run-and-tumble) of single *E. coli* cells in simple chemical gradients [6]. These models demonstrated how microscopic behavioral rules could impact the observed macroscopic movement. A multi-agent model was developed to explore chemotaxis in heterogeneous environments with physical obstacles, more recently by Proverbio (2024). The model demonstrated how decentralized gathering could emerge [34]. Although the implemented models are foundational and provide important insight into chemotaxis, they are focused on a single species or have limited environmental challenges and factors.

4.2 Modeling Microbial Competition and Social Dynamics

Interaction between cells is a critical aspect of microbial ecology. Biofilm formation is a key survival strategy and has been a major research point. Sweeney et al. (2019) developed an ABM that demonstrates how local chemotactic behavior directly shapes the formation of biofilms, an occurrence that continuum models struggle to represent [39]. Furthermore, models incorporating direct competition have been created, like the

individual-based model developed by Ni and Lu (2022) that simulates the spatial dynamics between two competing microbial populations, where one produces an inhibiting toxin [37].

4.3 Applied Models of Chemotaxis

Chemotaxis models are being used to solve applied problems in medicine and environmental science, not just as scientific research. In bioremediation, models have been developed and used to understand how bacteria can be harnessed to clean up pollutants [2, 9]. In the pharmaceutical domain, chemotaxis models are being created to design new therapeutic strategies, such as for targeted drug delivery [10].

4.4 Research Gaps and Contribution

Reviews of the field identify several persistent challenges in ABM. This research directly addresses these limitations in the following ways:

1. This project contributes a generalized and extensible framework that moves beyond the single-species or highly specific models, allowing simulations and comparisons of diverse bacterial species and environmental contexts.

2. A modular architecture was created with clearly defined components for bacterial agents, chemical environments, and physical obstacles, allowing for an easily extensible and adaptable model.

3. A competitive framework is implemented to enable multi-species interactions in heterogeneous environments, bridging the gap between models focusing solely on environmental complexity versus those examining competition in isolation.

5 Methodology

5.1 Model Design and Theoretical Framework

5.1.1 Agent-Based Modeling Approach

This research implemented an **agent-based model (ABM)** to simulate bacterial chemotaxis behaviour in competitive heterogeneous environments. The ABM was chosen due to its ability to showcase emergent behaviours from individual agent interactions as well as population heterogeneity, which is lost in continuum models [4, 3]. The model follows an individual modeling framework of microbial systems, where each cell is represented by an agent defined with its own properties and behavioral rules. NetLogo 6.4.0 was used to implement the model as its programmable multi-agent modeling environment was most fitting. NetLogos's integrated visualization and efficient handling of spatial interactions were also very beneficial for the model's construction and design.

5.1.2 Model Components and Architecture

The simulation architecture consists of four interconnected parts:

1. **Bacterial Agents**: Individual agents each representing a sole bacterial cell with species-specific properties.

2. **Environmental Contexts**: Parameter sets defining the context of the simulation. This context impacts the bacterial behaviours based on species-specific property interactions.

3. **Chemical Zones**: Dynamic gradient fields of attractants, repellents, and signaling molecules. These zones alter the environment by increasing nutrient levels as well as introducing toxins.

4. **Physical Obstacles**: Impermeable or semi-permeable barriers creating heterogeneous spatial constraints impacting movement and chemical gradient sensing.

The model follows a **modular design principle** where each component can be independently parameterized and extended.

5.2 Bacterial Agent Implementation

5.2.1 Species Selection and Parameterization

Seven bacterial species were selected based on **ecological relevance**, **pharmaceutical significance**, and property diversity (See Background, Table 1a & 1b). Species parameters were derived from empirical literature and included in a CSV data file ('bacteria.csv') for modular management.

5.2.2 Movement Algorithm

Bacterial motility was implemented using a **biased random walk algorithm** that alternates between *running* and *tumbling* states, following the established framework for bacterial chemotaxis simulation [6, 47]. The core of the advantage that chemotaxis sensing provides is derived from movement decision-making. The decision process follows this computational procedure:

```
Procedure: calculate-best-tumble-direction
1. Sample chemical potentials at 8 directions within the sensing
   radius.
2. Calculate attraction score: sum(potentials of attractants).
3. Calculate repulsion score: sum(potentials of repellents).
4. Compute net chemical score: attraction_score - repulsion_score.
5. If the net score is not better than the current, seek local
   nutrients.
6. Incorporate momentum (40% weight).
7. Incorporate social attraction (30% weight if swarming).
8. Return optimal heading direction.
```

The algorithm uses the species-specific properties defined in 'bacteria.csv' to determine sensing radius, and the chemotaxis scores based on species-specific attractants and repellents. The behavior of the bacteria changes based on internal and environmental conditions, transitioning between normal foraging, biofilm-seeking, and biofilm-resident states.

5.2.3 Bacterial implementation

Each bacterial agent maintains internal state variables, including:

- **Energy level**: Decreased by movement and chemical production and replenished by nutrient consumption, with a maximum of 100 and a minimum of 0.
- **Toxin load**: Accumulated from environmental toxins and slowly decreased over time.
- **Age**: Tracks cellular lifespan and triggers reproduction as well as death due to old age.
- **Biofilm status**: Determines metabolic costs and behavioral patterns.
- **Movement status**: Determines if the agent is currently *running*(moving forward) or in a tumble state, thus busy with movement direction calculations.

Each bacterial agent has properties with values determined by species type. The properties determine the agent's behaviours and interactions.

- **Attractants**: A list of chemicals that the bacterial agent can sense and is attracted to.
- **Repellents**: A list of chemicals that the bacterial agent can sense and is repelled by.
- **Speed**: Determines how far an agent can move per time period.
- **Run/Tumble Durations**: Used to determine distance travelled based on speed, as well as determine state timers.
- **Taxis Sensitivity**: The radial distance in which an agent can sense chemical gradients.
- **Energy Source**: Determines how the oxygen levels of the environment impact the bacteria's performance and energy uptake.
- **Lifespan**: The maximum amount of time a bacterial cell can survive without reproducing.
- **Division Rate**: The rate at which the bacterial agents can split into two new cells. This is used as the age of the bacteria from when the cell can reproduce.
- **Stress Tolerance**: Determines the amount of toxins an agent can handle before dying, as well as the impact unpreferred pH levels have on the bacterial cell.
- **Biofilm Forming**: Determines whether the agent can form biofilm structures.

- **Swarm Behaviour**: Determines whether the agent shows swarming behaviour with movement decisions in a population.
- **Preferred pH**: The optimal environmental pH of the bacterial agent impacts its movement speed, energy obtained from nutrient consumption.
- **Size**: The size of the bacterial agent. Used to represent the cell to scale in the scaled environment.
- **Procuced Chemicals**: The list of chemicals the bacterial agent can produce. Chemicals listed here are handled with species and chemical-specific algorithms.
- **Gram Stain**: The Gram typing of the bacteria; either gram-posistive and gram-negative. This trait is used to determine whether toxins impact the bacterial cell based on the toxin's own property specifications.
- **Colour**: A colour chosen purely for visualisation purposes.

Energy consumption rates were parameterized differently for planktonic ('energy-cost-normal') and biofilm-associated ('energy-cost-biofilm') states, with biofilms depleting energy much more slowly while also being static. When bacteria are low on energy (less than 30), they enter a seeking biofilm state. They then produce the chemical Autoinducer-2, which other biofilm-seeking bacteria are attracted to. When the seeking bacteria come together, they form an energy-efficient biofilm structure to extend their lifespan in the harsh conditions. *Paenibacillus polymyxa* is the only species that produces a different chemical in the current model. *P polymyxa* produces the toxin Polymyxin B, a toxin affecting gram-negative bacteria. They produce the chemical when the *P polymyxa* cells are in high density, have high energy levels, and there are competitive agents nearby.

5.2.4 Environment Implementation

Four distinct environmental contexts were implemented (See Background, Table 3a & 3b), each with specific physicochemical parameters affecting bacterial behavior. The environment parameter information is loaded from the 'environments.csv' file. These parameters determine the context of the bacterial simulation, affecting bacterial performance and behaviors.

- **Scale**: Determines the area that one patch represents in the model. item **Time/Tick**: Represents the amount of time simulated with each passing tick.
- **pH**: Provides the pH value of the simulation impacting bacteria's fitness.
- **Oxygen Level**: Describes the type of environment in the context of oxygen abundance, affecting bacterial fitness based on their energy source trait. For example, a hypoxic (low-oxygen) environment will put aerobic (need oxygen) bacteria at a great disadvantage.
- **Viscosity**: This property modifies the movement speed of all bacterial agents. This simulates the difference of moving through a liquid like water or the gel of an agar plate.
- **Nutrient Availability**: This sets the starting nutrient level of the environment. For example, a nutrient-abundant environment will have much higher general nutrient concentration than an environment with scarce nutrient availability.

5.2.5 Chemical Implementation

The chemical implementation is a critical component of the model as it provides the chemotactic cues to which the bacterial agents should react. Six different chemicals were implemented, each with a different set of properties loaded from the 'chemicals.csv' file. Chemical diffusion is simulated and handled with NetLogo's built-in 'diffuse' primitive, which creates dynamic gradients across the environment. The chemical implementation was simplified as to focus on chemotactic signalling rather than a complete chemical simulation. For later research, the chemical realism in the model can be enhanced. Each chemical is defined by the following properties:

- **Type**: Categorizes the chemical as an **Attractant**, **Repellent**, or **Quorum signal**, determining how bacteria will react to its presence.
- **Toxicity**: Defines how harmful the toxin is; a higher toxicity means the affected bacteria's toxin level increases more per tick.
- **Metabolizable**: A boolean value that determines whether the chemical increases nutrient levels in its zone or if it creates a toxic zone. This was done to simplify the simulation.
- **Target Gram Type**: For toxic chemicals, this specifies which type of bacteria are affected. It can be either **Gram-positive**, **Gram-negative**, or **Both**, allowing for the simulation of targeted antimicrobial agents like Polymyxin B.
- **Colour**: A colour chosen purely for visualisation purposes.

The simulation of chemical dynamics follows a clear procedure, ensuring that gradients are constantly evolving in response to diffusion, decay, and bacterial interaction.

```
Procedure: update-chemical-potentials
1. Initialize chemical potentials for all patches based on local
   concentrations.
2. Apply source contributions and natural decay (e.g., 5% per time
   step for AI-2).
3. Diffuse each chemical potential according to its diffusion
   coefficient.
4. Repeat the diffusion process 10 times per tick for gradient
   smoothing.
```

5.2.6 Obstacle Implementation

To create more complex and heterogeneous environments, five types of physical obstacles have been saved and can be loaded from 'obstacles.csv'. These obstacles directly affect bacterial movement as well as their chemical sensing abilities. The obstacle properties are implemented as follows:

- **Size**: Defines the physical footprint of the obstacle within the environment, with its size scaling with the environmental scale.

- **Permeability**: Indicates how harshly bacterial movements are impacted by the obstacle. A permeability of 1 would mean the bacteria cannot move through the obstacle.
- **Toxicity**: If an obstacle is toxic, it increases bacterial toxin levels when the agents come in contact with the obstacle.
- **Colour**: A colour chosen purely for visualisation purposes.

5.2.7 Initialization and Setup

The model initialization follows a sequential procedure:

```
Procedure: setup
1. Load parameter files (bacteria.csv, chemicals.csv, etc.).
2. Configure world dimensions and scaling.
3. Initialize environment with selected parameters.
4. Create chemical sources based on user configuration.
5. Initialize bacterial populations in specified zones.
6. Place obstacles according to configuration.
7. Reset trackers.
8. Update visualization.
```

Chemical zone size scales with the dimensions of the environment. Bacteria size representation can be switched between not scaling with the environment scale, being represented as uniform circles, and being represented to scale based on their species-specific size. When the bacteria are scaled, the patches represent the bacteria with gradients based on bacterial densities, due to the scale quickly rendering the bacteria too small to visualize. Obstacles also scale with the environmental scale, with their size changing based on scale size. The obstacles are placed on top of the environment, being the dominant occurrence and overwriting selected parameters if needed.

5.2.8 Time Stepping and Agent Updates

The simulation employs updates to agents and patches per tick. The impact of each tick is determined by the 'tick-duration-s' value, as this determines how much time passage is employed per tick.

```
Procedure: go
1. Chemical production by bacterial agents (e.g., AI-2, Polymyxin B).
2. For each bacterium:
    - Update energy and age.
    - Interact with the environment (nutrient uptake, toxin exposure).
    - Execute state-based behavior (run, tumble, seek-biofilm).
        - Tumble and seek-biofilm calculates the best movement
          direction.
    - Check for reproduction (if energy and age criteria are met).
    - Check for death (starvation, old age, toxin overload).
3. Remove dead agents.
4. Record data and update visualization.
```

```
5. Update chemical potentials (diffusion and decay).
6. Advance simulation clock.
```

5.2.9 Behavioral State Machine

Bacterial behavior is determined by a state system that changes based on temporal and internal cues.

1. **running**: Forward movement based on speed, scale, and time/tick.
2. **tumbling**: Direction calculation based on chemotactic cues, nutrient levels, and swarming.
3. **Seeking-biofilm**: Directed movement toward AI-2 signals to attempt to form biofilm structures, when energy levels are low.
4. **In-biofilm**: Reduce energy usage as well as create more robust stationary structure.

5.2.10 Data Collection and Analysis

The model tracks bacterial and environmental counts to provide a graphical analysis.

- **Population metrics**: Total and species-specific population counts over time.
- **Physiological metrics**: Average energy and toxin levels of bacteria species.
- **Behavioral metrics**: Number of bacteria in biofilm.
- **Mortality metrics**: Total bacterial deaths categorized by causes, starvation, old age, and toxin.

5.3 Model Validation Approach

To validate the models performance the following tests were conducted.

5.3.1 Quantitative Validation: Population Growth Dynamics

In a closed system, bacterial colonies follow a predictable logistic (S-shaped) growth curve [48]. Thus, it is important to tests that the model replicates this growth curve in a closed, resource-limited environment. The test ensures that the bacteria's basic metabolic and reproduction functionality works as intended.

5.3.2 Qualitative Validation: Pattern Matching

To validate the model's ability to replicate known patterns that emerge due to the collective behavior of agents, we test for the formation of radial swarming rings by *E. coli* [15]. This is a well-documented macroscopic phenomenon that occurs when the *E. coli* depletes the center resources and then moves outward in a ring. Matching this occurrence indicates that the chemotaxis algorithm functions accordingly and is integrated into environmental and metabolic modules effectively.

5.3.3 Behavioral Validation: Negative Control

This test ensures that the impact we observe is due to the factor we are testing [49]. For this test, we compare simulations where the chemotaxis functionality is turned off with simulations where the agents have chemotaxis abilities. This test ensures that the foraging ability is linked to the chemotaxis algorithm and not other factors.

5.3.4 Ecological Validation: Competitive Exclusion

To validate the model's ability to simulate multi-species interactions with the competitive exclusion principle, we simulate two bacteria species: the toxin-producer *P. polymyxa* (Gram-positive) and the susceptible *B. cenocepacia* (Gram-negative). The competitive exclusion principle is an important cornerstone for ecology[50]. Theoretically, the *P. polymyxa* occupy the nutrient-rich zones while the *B. cenocepacia* colonies are stuck in limited zones due to being repelled by the Polymyxin B toxin that is produced. Seeing this behavior ensures the credibility of the multi-species interactions.

5.3.5 Robustness Validation: Complex Environment Test

For the final validation test, we want to ensure the model's ability to simulate a more complex environment. This test is important to see that the multiple parts and variables of the model correctly interact with each other.

6 Discussion

This research set out to develop a generalized, agent-based framework for simulating multi-species bacterial chemotaxis in complex, competitive environments. The resulting model, implemented in NetLogo, successfully integrates the core modules of bacterial agents, a dynamic chemical environment, physical obstacles, and distinct ecological contexts. This section discusses the validation of the model's core mechanics, presents the results of several computational experiments designed to address the research questions, and explores the broader implications of these findings.

6.1 Model Verification and Validation

Before using the model for scientific inquiry, a multi-stage validation and verification process was conducted to build confidence in the model as a credible representation of microbial systems. This process progressed from verifying internal logic to validating emergent behaviors against quantitative, qualitative, and theoretical benchmarks.

6.1.1 Quantitative Validation: Population Growth Dynamics

A fundamental test for any bacterial population model is its ability to reproduce the standard S-shaped (sigmoidal) logistic growth curve as shown in figure 1. The population growth curve shown in Figure 2 provides an indication that the simulation is capable of simulating a population that simulates the four key phases(Lag Phase, Exponential growth phase, Stationary phase, and Death phase) of a bacterial growth curve in a closed, nutrient-rich environment. For this test, a starting colony count of 31 E.coli cells where

placed in the center of an agar plate environment. The match between the example and the obtained curve validates the model's core metabolic and reproductive mechanics.

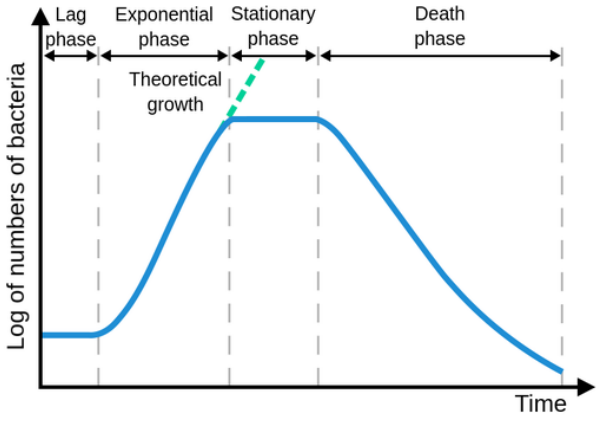

Figure 1: Example of growth curve of a single bacterial colony in a closed system [48].

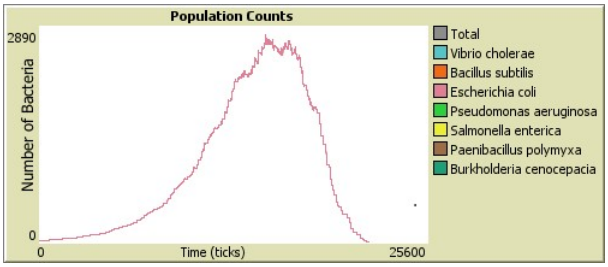

Figure 2: Population dynamics of a single *E. coli* colony of starting size 31 in a closed system, demonstrating a close fit to the theoretical logistic growth curve. This test was run with a world size of 121x121, with each patch representing a 100μmx100μm area. The simulation ran for 21685 ticks, with each tick representing 0.1 seconds.

6.1.2 Qualitative Validation: Pattern Matching

Due to bacteria population expanding in a predictable manner, it is important to verify that the model is able to replicate that growth.*E. coli* grows in a radial pattern as the colony depletes nutrients in the center and grows outward, as shown in Figures 3. To simulate this growth pattern, a starting colony of 31 *E. coli* cells were placed in the center of an agar plate environment. Each patch represents 100μmx100μm area and each tick 0.1 seconds of passing time. The starting colony was placed in the center of a glucose gradient zone to provide abundant nutrients. Figures 4 and Figures 5 show the circular pattern emerging as the bacterial colonies grow. Figures 4 show the simulation with the bacteria represented to scale in the environment, and Figures 5 do not rather allowing us to observe the bacteria as individuals. The model successfully replicated the circular outward growth pattern as the central nutrients depleted, indicating the model's ability to simulate bacterial movement patterns.

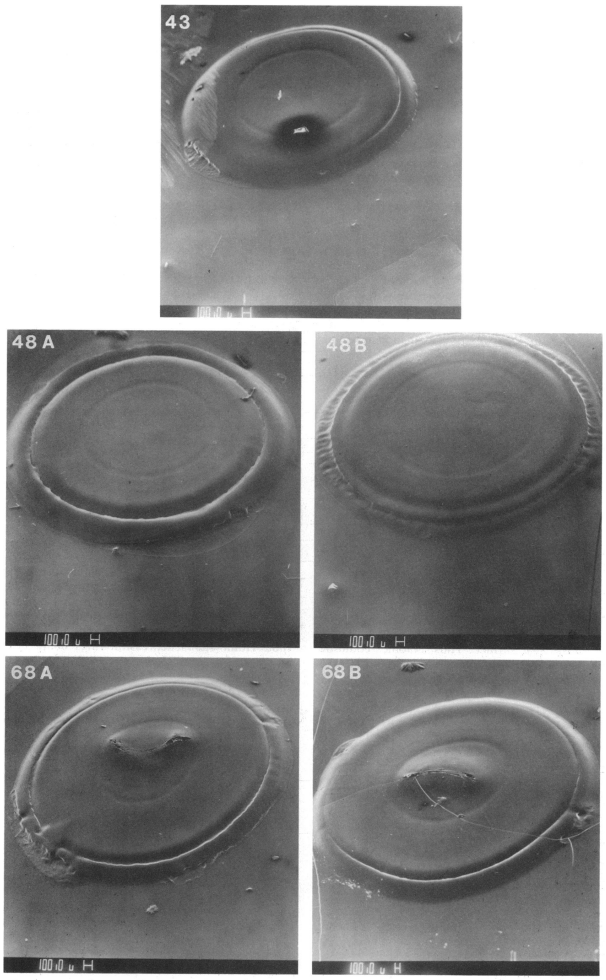

Figure 3: Example of E.coli growth patterns in a closed agar plate environment [51].

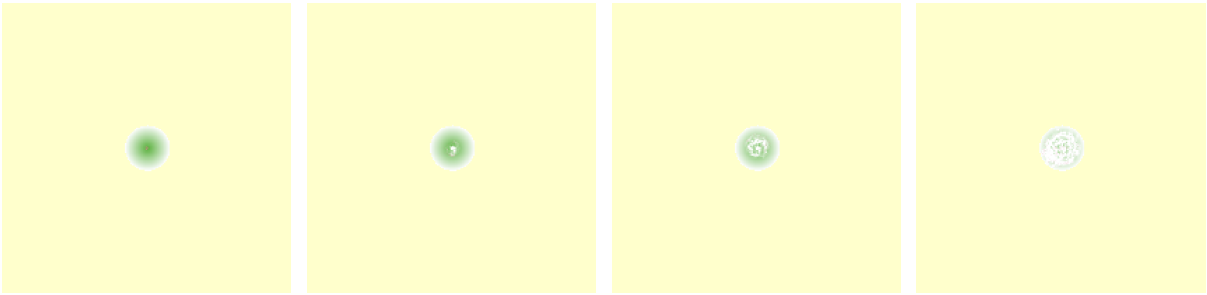

Figure 4: Validation experiment replicating the emergent swarming ring of *E. coli* with bacteria represented to scale, visualized by density.

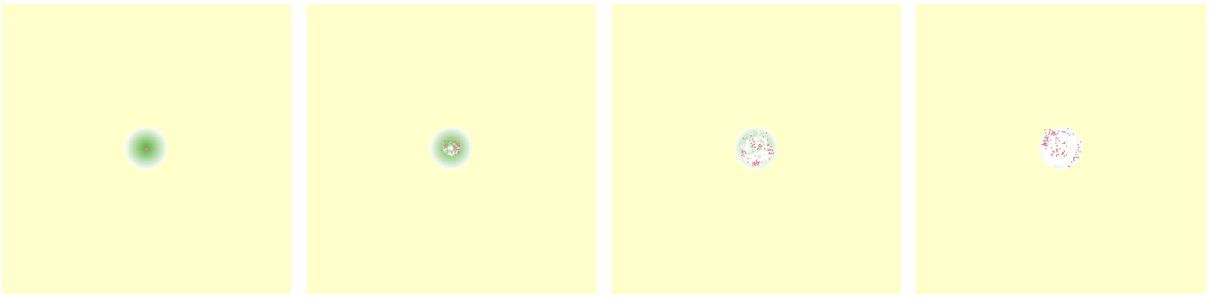

Figure 5: Validation experiment replicating the emergent swarming ring of *E. coli* represented with bacteria not shown to scale to show individual movement.

6.1.3 Behavioral Validation: Negative Control

To confirm the chemotaxis algorithm provides the expected functional advantage, a negative control experiment was conducted. Four populations of *E. coli* were simulated, a pair with chemotaxi functionality on and a pair with it turned off. Both pairs had one simulation with bacteria size to scale and one without cell size to represent to scale. These simulations were simulated in an agar plate environment with a 101x101 grid size, with a patch representing a 100μmx100μm area and each tick 0.1 seconds of passing time. The *E. coli* starting colonies of size 1038 were randomly placed in the environment. Eight glucose sources (*E. coli* attractant and high nutrient source) and eight phenol sources (*E. coli* repellent and toxin) were randomly placed inside the environment.

- In **Figures 8 and 9** it can be seen a clear movement towards the glucose sources and the avoidance of the phenol sources.
- **Figure 6** shows a very uniform and stable population curve with a maximum population count of 3640 cells, with cells alive up to 8380 ticks.
- In **Figures 10** and 11, there is searching for glucose and avoidance of phenol, which leads to bacteria entering the toxic zone and dying, and bacteria dying due to starvation with glucose nearby.
- **Figure 7** shows a very uniform and stable population curve with a maximum population count of 2740 cells, with all cells dying off around 8000 ticks.
- **Conclusion**: The chemotaxis algorithm provided a functional advantage as observed with the much higher and stable population growth in the tests, where the *E. coli* cells had chemotactic abilities than in the test where they did not have the chemotaxis functionality. This observation indicates the working state of the model's chemotaxis algorithm.

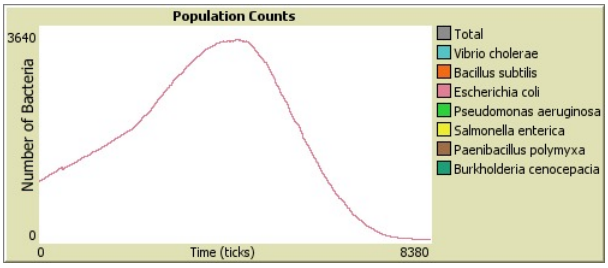

Figure 6: Population growth graph after 8380 ticks with chemotaxi functionality.

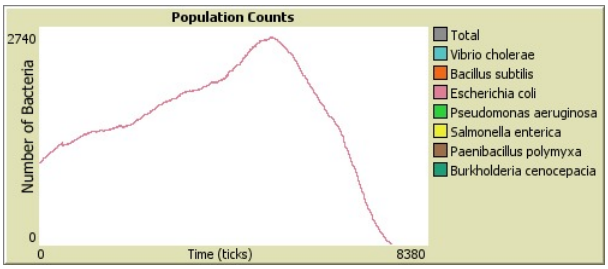

Figure 7: Population growth graph after 8010 ticks with chemotaxi functionality turned off.

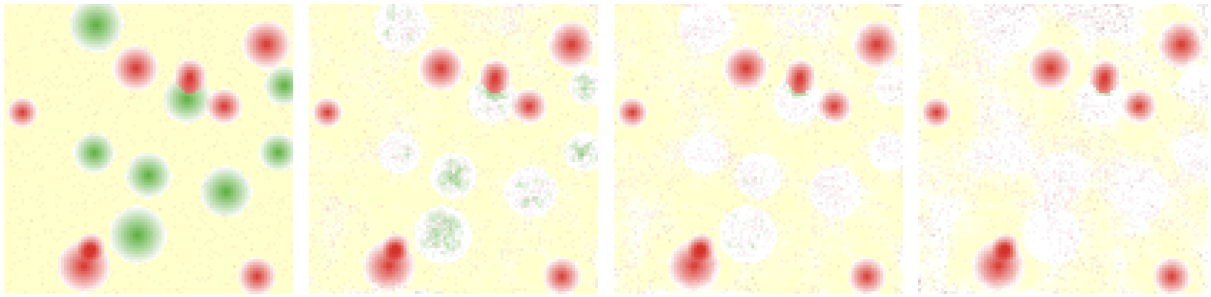

Figure 8: *E. coli* growth and movement with chemotaxis and cell size to scale.

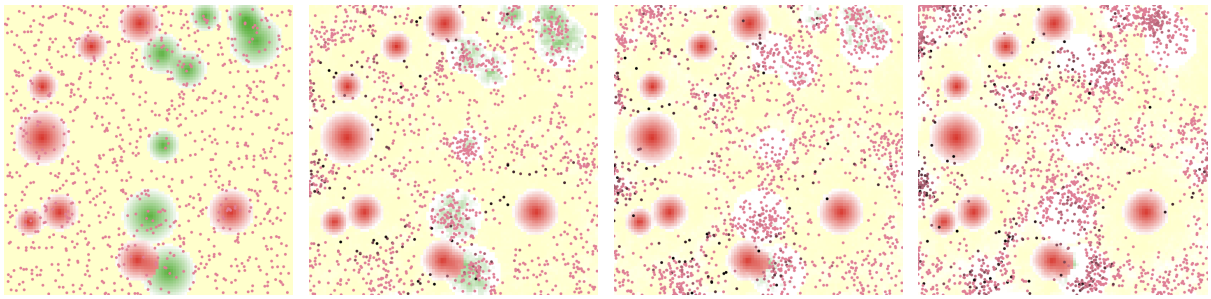

Figure 9: *E. coli* growth and movement with chemotaxis and cell size not to scale.

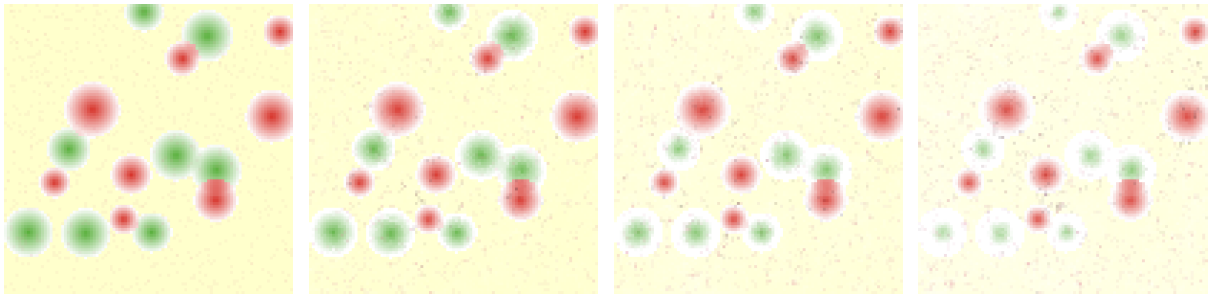

Figure 10: *E. coli* growth and movement with no chemotaxis impact and cell size to scale.

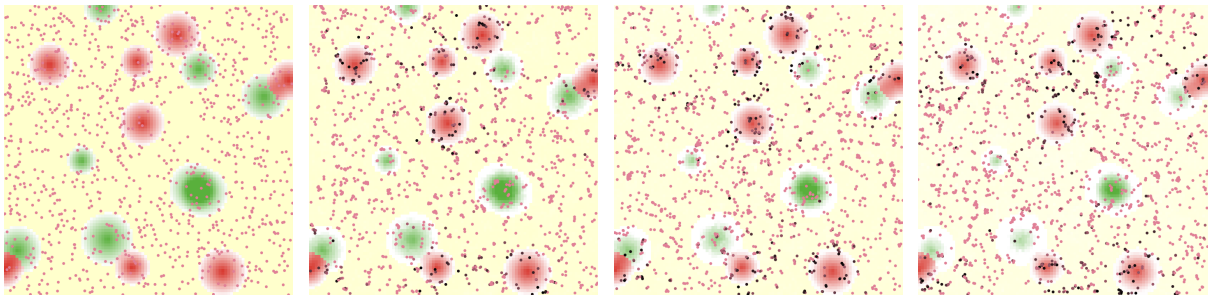

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Figure 11: *E. coli* growth and movement with no chemotaxis impact and cell size not to scale.

6.1.4 Ecological Validation: Competitive Exclusion

To validate a multi-species simulation, we must test a competitive exclusion scenario. For this co-culture *P. polymyxa*, a toxin producing bacteria, and *B. cenocepacia*, a bacterium susceptible to the produced Polymyxin B toxin but also repelled by it. The simulation is done with an agar plate environment of size 71x71 with a patch area of 50μmx50μm. Each tick represents 0.1 seconds of passing time. Both starting colonies had a starting count of 150 that were randomly placed as shown in Figure 12. Eight sources of both Glucose and Phenol are randomly placed. At 500 ticks(Figure 13), both bacteria were at the glucose sources and *P. polymyxa* had started producing Polymyxin B (Pink). In Figures 14 we can see how *B. Cenocepacia* is excluded and is stuck in limited areas due to the produced toxins. From figure 15 it cis observed that the *P. polymyxa* population had much better growth due to their ability to repel *B. cenocepacia* from the Glucose zones by producing Polymyxin B. rom these observations, the model's ability to simulate multi-species competition is validated to simulate multi-species competition.

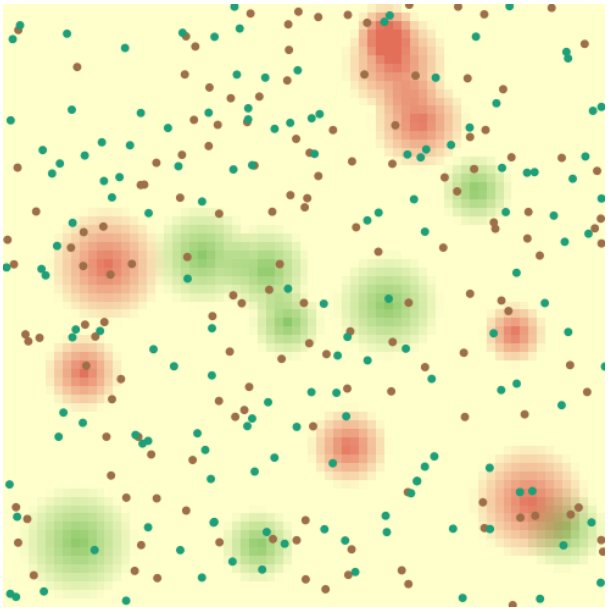

Figure 12: Both bacteria were randomly dispersed in the environment to prevent a preset advantage, shown not to scale.

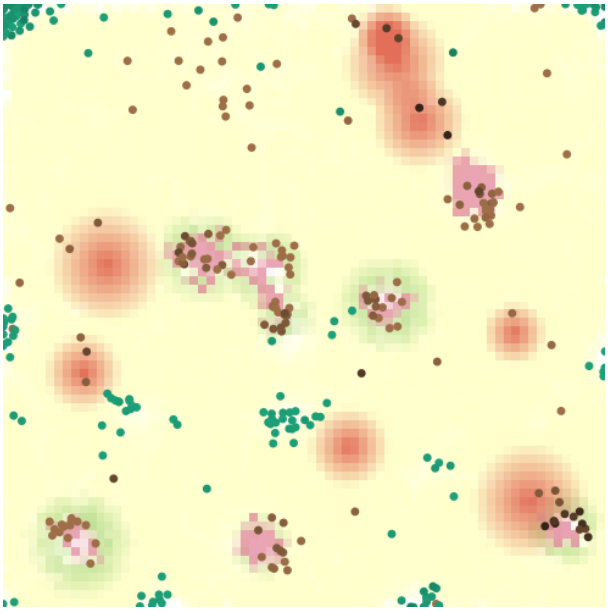

Figure 13: At 500 ticks, Polymyxin B (pink) is being produced near glucose zones (green).

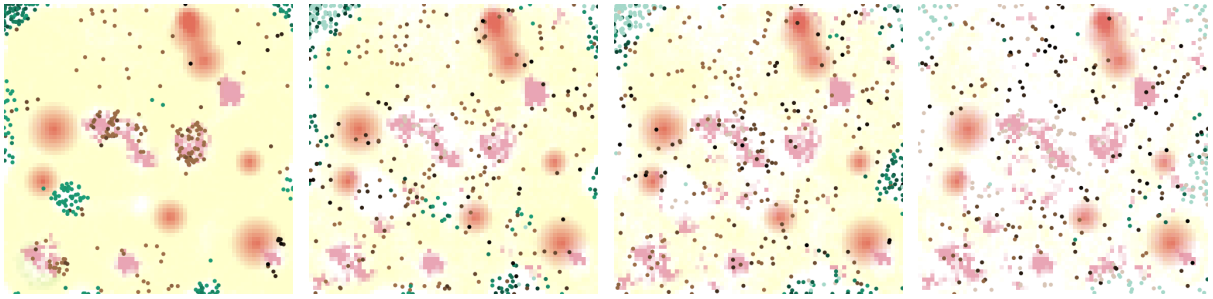

Figure 14: Competitive exclusion created due to Polymyxin B production over time, shown not to scale.

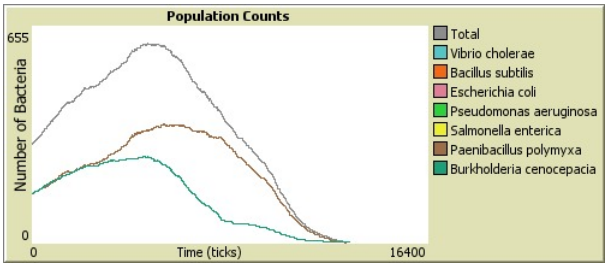

Figure 15: Population growth graph of *P. polymyxa* and *B. cenocepacia*.

6.1.5 Robustness Validation: Complex Environment Test

Ensuring the models' performance in a more complex environment is important. For this test, a wound site environment was simulated in a 100x100 grid containing 30 necrotic tissue obstacles as well as five asparte zones, both randomly distributed. The patches represented a 70μmx70μm area, and the ticks represented 0.1 seconds of passing time. The bacteria *P. aeruginosa* and *S. enterica* had starting colony sizes of 50, and were placed at the center of the simulation. These bacteria were chosen to represent the effect of oxygen levels on the different types of bacteria. The wound site environment is hypoxic. Thus *P. aeruginosa* has a great disadvantage being aerobic, while *S. enterica* is unfased, being facultative. Both these bacteria are attracted to aspartate; thus, it was chosen to provide the chemical gradients. Figure 16 shows the starting point of the simulation. In Figures 17 and Figure 18, we see how the *P. aeruginosa* quickly dies off due to the lack of oxygen, while *S. enterica* slow grows and colonizes. The necrotic-tissue obstacles hinder the spread of the *S. enterica* cells, but the population is observed to be slowly following chemical gradients and finding the aspartate zones. Figure 18 indicates the effectiveness of the model to simulate different types of bacteria with different needs in a complex environment.

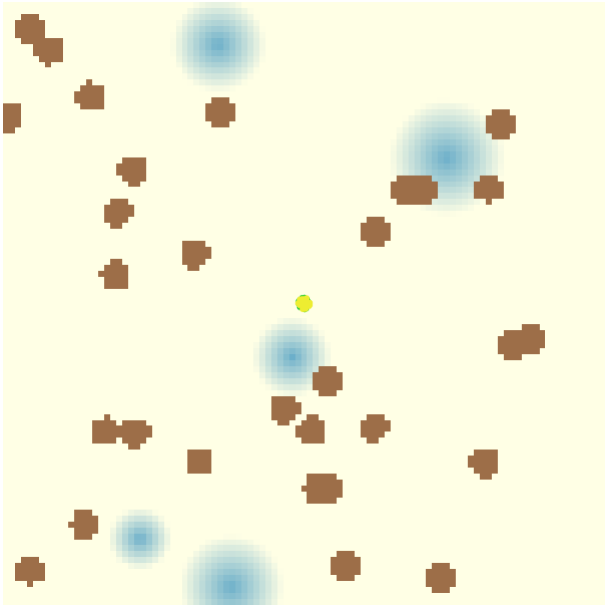

Figure 16: Initial layout of complex environment simulation of a wound site containing *P. aeruginosa*, *P. aeruginosa*, necrotic tissue, and aspartate, shown not to scale.

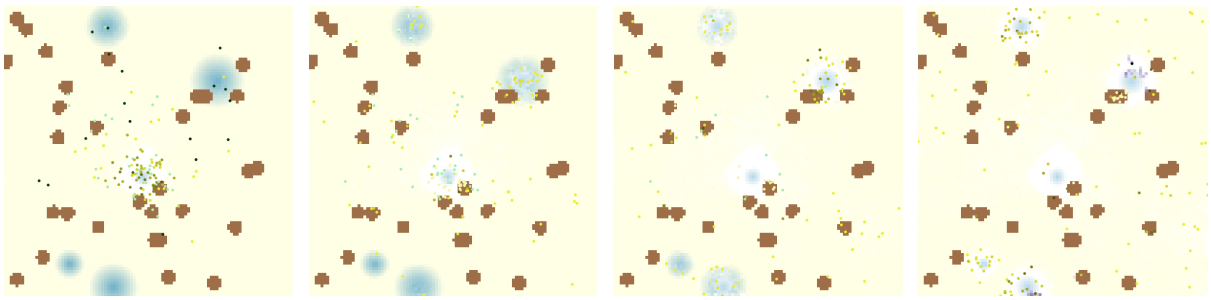

Figure 17: Growth and spread of bacterial colonies in a complex environment, shown not to scale.

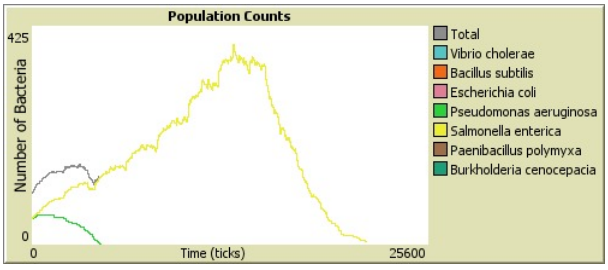

Figure 18: Population growth graph of *P. aeruginosa* and *S. enterica* in a complex wound site environment.

6.2 Limitations of the Model and Future Work

While this model provides a robust framework, this model still has limitations and avenues that are unexplored.

- **Two-Dimensional Representation:** This model only simulates a 2D environment, real life bacterial life exists in a 3D environment and biofilms for 3D structures as noted by Sweeney et al. (2019) [39].
- **Simplified Metabolism:** The model's metabolic process is a simplified version of metabolic pathways, with chemicals interacting as food sources in the same way. It is important to expand the model to accurately simulate how bacteria interact with glucose specifically, as it is different than aspartate, for example.
- **Genetic Adaptation:** The model does not simulate the mutation of bacteria; expanding on this area is important because bacteria adapt to environments over long periods of time.
- **Hydrodynamics:** The model does not simulate flow dynamics. Implementing flow into the model would be beneficial to simulate more dynamic environments, like lake water, more accurately.
- **Expanding Library:** Increasing the dataset of the model will allow more complex and accurate simulations.

7 Conclusion

This study addressed the need for a generalized, modular, and extensible model capable of simulating the dynamics of competitive multi-species microbial communities in complex, heterogeneous environments. This was achieved in this research by implementing an Agent-Based Model (ABM), developed using NetLogo. The developed framework effectively bridges the gap of previous models by combining the strengths of models focused on environmental navigation with those that typically study competitive interactions within highly simplified spaces. By allowing individual agent-level decisions to collectively drive the behavior of the entire population, the ABM facilitates validated lifelike simulations.

The model's robustness was confirmed with multi-stage validations. These tests demonstrated the model's ability to reproduce several key emergent bacterial behaviors, including the logistic growth curve of a population, chemotactic swarming patterns, and the principle of competitive exclusion. The models were shown to be able to simulate a realistic, multi-species scenario within a heterogeneous wound environment.

Currently, the model is constrained to a 2D environment, as well as simplified metabolism and chemical interactions. The modular design of the model offers a clear path for future expansion. This includes incorporating evolutionary dynamics and introducing fluid dynamics. Ultimately, this research forms a starting point to showcase that developing a robust virtual lab is possible and would prove very beneficial in clinical and bioremediation applications.

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