

STOCHASTIC MODELLING OF A CHEMOTACTIC MICROSWIMMER

M.Sc Thesis by
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Knowledge is Freedom

Theoretical Physics Stream

African University of Science and Technology, Abuja

November, 2011

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Abstract

Key to *Escherichia coli* (*E-coli*) bacteria survival is its ability to direct its movement to greener pasture and flee harmful environment - also known as *chemotaxis*. This thesis focuses on the modelling of *E-coli* chemotaxis in two-dimensions with emphasis on trying to understand the basic physics of how such a tiny microswimmer swim up a concentration gradient despite the enormous thermal fluctuations in its environment. *E-coli* strategically employs near straight swimming (also known as *run*) often interrupted by random re-orientations (also known as *tumble*). How often this interruptions happens is the swimmer tumbling frequency. This chemotaxis strategy is here modeled as random telegraph process, which is a dichotomous stochastic process. The swimmer tumbling frequency is represented as the transition rate from *run* phase to *tumble* phase. The transition rate is a function of swimmer specific trait (known as response kernel) and the environmental condition - concentration profile. Furthermore, the random telegraph process is coupled to the swimmer Langevin equations in which the system was solved analytically making judicious approximations. Important chemotaxis parameter expression was obtained for a swimmer with arbitrary trait and a simple swimmer case scenario analyzed. Even though, this framework describes *E-coli* chemotaxis excellently, it can as well serve as a base framework for study of other interesting models that exhibit two state swimming strategy.

Acknowledgments

I would like to sincerely thank my supervisor Prof. Tanniemola B. Liverpool, University of Bristol, for his continuous guidance throughout the course of this work. I deeply appreciate him introducing me to this exciting area of research, which was prior unknown to me. Many thanks goes to Dr. Margaritis Voliotis of Applied Mathematics Department, University of Bristol, for his prompt response to questions and valuable suggestions throughout this work.

This thesis would have not been a reality without the continuous moral support, love and care of my Mom, Saudatu Ibrahim Sarki, my wife A'isha Umar Tambaya and the entire family.

Thank you Rashidi Salako, Maruf Minjibir, Edwin Soh of Pure and Applied Mathematics stream, Mustapha Abdu-Aguye - Theoretical Physics stream, Obinna Ezuiluke - Petroleum Engineering stream, Larry Godwin - Computer Science stream, all of AUST for nice discussions and motivation. Thank you all and more grease to your elbows.

I would like to thank Petroleum Technology Development Fund (PTDF), for the full support of my studies here at AUST.

(All ideas, concepts, figures taken from other sources, such as books, journal articles are fully referenced herein.)

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Chapter 1

Introduction

The ability of a living organism to direct its movement up or down a chemical gradient is termed *chemotaxis*. This thesis focuses on modelling *Escherichia coli* (*E-coli*) chemotaxis in two dimensions. *E-coli* bacteria lives in aqueous environment such as our intestine. It is quite challenging for a tiny organism like bacteria that knows nothing about inertia to find food in such aqueous environments. Motile (flagellated) *E-coli* evolves strategies to manoeuvre themselves to regions of high concentrations of a chemical attractant (chemoattractant) and moves away from chemical repellent (chemorepellent) [1–3]. The strategy involves *runs*; which are near-straight swimming along its principal axis, and *tumble*; which are random re-orientation (erratic movement) in same neighborhood. This mystic mechanism of bacterial chemotaxis had attracted a lot of attention in the scientific community in last few decades [1–5]. Currently, there is intensive thrust towards design and fabrication of artificial microswimmers (micro- and nano-swimmers) - mimicking nature to accomplish important tasks [6–8]. Man-made microswimmers holds the promise of revolutionising medicine, such as in drug-delivery and early disease detection [6].

Chemical molecules in the hydrodynamic environment binds to chemoreceptors distributed over the *E-coli* cell membrane. The cell analyses the

signal through its biochemical pathways (feedback loop) and respond via its motility machinery [1–3]. It changes the direction of the flagella rotation from clock-wise direction (CW) to counter-clock-wise direction (CCW) periodically depending on the chemical (chemoattractant or chemorepellent) sensed or intercepted over some characteristic time scale. Smooth runs corresponds to CCW- and tumbles corresponds to CW-rotations of its flagella [1]. Consequently, the switching of the flagella direction of rotation results in longer runs in case its moving towards a region of high concentration and shorter when moving in the opposite. Through tethering assays of *E-coli* cell, it was found that it is unlikely the cell will make spatial measurements of concentration gradient but rather it will sample the space and average the detections over time, in other words it makes temporal comparisons of the most recent measurements [1, 5]. The response function that fits good with the experimental data was determined by Celani and Vergassola [9] using game theoretic approach. Celani and Vergassola showed that the response was selected as a maximin strategy of the *E-coli*, i.e highest minimum uptake of chemoattractant for any concentration profile. This strategy ensures good response to any concentration profile for a microswimmer in a complex environment (where the microswimmer is subject to conflicting response requirements).

In molecular scales, the microswimmer exhibit stochastic motion due to fluctuations in its environment. In addition, random torques can significantly affect the swimmer motion [1]. Artificial microswimmers recently developed (e.g spherical Janus particles) with additional asymmetry demonstrates significant gain in translational displacement [10]. However, these microswimmers do not mimick the *E-coli* chemotaxis strategy directly. Hence, we have so far achieved only partial control of these swimmers. The question remains, how a swimmer swim up the chemoattractant concentration gradient despite the thermal fluctuations? - taking note of the fact that engineered devices usually have small number of degrees of freedom. What strategy a swim-

mer should employ to extract directed motion from the ceaseless noise with minimal internal degrees of freedom? Here, random telegraph process (as decision making process) is incorporated into the microswimmer's associated Langevin equations (for a microswimmer moving with a net deterministic velocity subject to Brownian randomization) and the resulting dynamics analyzed under different environmental conditions (concentration profiles).

Chapter 2

Background Literature

This chapter will briefly introduce some of the most important stochastic calculus concepts used throughout this thesis. It will serve as a quick reference to readers that are not so familiar with these concepts. In addition, we introduce a holistic overview of *E-coli* chemotaxis and some leading theoretical principles underlying the realization of a controllable synthetic microswimmer. (See the referenced works therein for detailed information)

2.1 Stochastic Processes

Counterpart to a deterministic system, such as rotating wheel, a stochastic system evolves probabilistically over time. They are usually characterized by a random variables $\mathbf{X}(t)$. The random variables takes values x_1, x_2, x_3, \dots at different times t_1, t_2, t_3, \dots respectively [11, 12], with an assumed joint probability distribution

$$P(x_1, t_1; x_2, t_2; x_3, t_3; \dots)$$

that completely describe the stochastic system. How present state of the system relates to the past and future states determines the different categories

of random processes. For example, a Poisson process in which the present is independent of the past and the future. Thus, the joint probability of this process is

$$P(x_1, t_1; x_2, t_2; x_3, t_3; \dots) = \prod_i P(x_i, t_i) \quad (2.1)$$

A Markov process is a stochastic process in which the present depends only on the most recent past and has finite or countable possible states (configuration space). The conditional probability for a system that is characterized by this property is

$$P(x_1, t_1; x_2, t_2; x_3, t_3; \dots) = P(x_1, t_1 | x_2, t_2) P(x_2, t_2 | x_3, t_3) \dots P(x_{n-1}, t_{n-1} | x_n, t_n) \quad (2.2)$$

with $t_1 \geq t_2 \geq t_3 \dots t_{n-1} \geq t_n$

Moments

The first and second moments of a stochastic process are the *mean* and the *correlation* of the measured random variable $X(t)$; such that the mean is

$$\langle X(t) \rangle = \int_{-\infty}^{\infty} x P(x, t) dx \quad (2.3)$$

while the correlation function is

$$C(t_1, t_2) = \langle X(t_1) X(t_2) \rangle = \int_{-\infty}^{\infty} dx_1 \int_{-\infty}^{\infty} dx_2 x_1 x_2 P(x_1, t_1; x_2, t_2) \quad (2.4)$$

These two moments are the ones mostly used in all averaging of fluctuations in this thesis.

Wiener Process(Brownian Motion)

A Wiener process $W(t)$ is an example of a Markov process that satisfies the following properties [12, 13]

-
1. $\langle W(t_0) \rangle = 0$
 2. $W : t \rightarrow W_t$ is almost surely continuous
 3. $\langle W(t_1)W(t_2) \rangle = C(t_2 - t_1)$

Random Telegraph Process (RTP)

This is a process that switches between only two states with certain transition rates (probability per unit time) associated to each state [11]. A set of equations governing the evolution dynamics of this process (also called Master equations) are

$$\partial_t P_1(t) = -\mu(t)P_1(t) + \lambda(t)P_2(t) \quad (2.5)$$

$$\partial_t P_2(t) = \mu(t)P_1(t) - \lambda(t)P_2(t) \quad (2.6)$$

$P_1(t) \equiv P(\alpha_1, t)$ and $P_2(t) \equiv P(\alpha_2, t)$ are probabilities of finding the system in state α_1 and state α_2 at any time t respectively. $\mu(t), \lambda(t)$ are the transition rates (could generally be a function of time as emphasized by the time-dependence).

2.2 Langevin Equation

Stochastic differential equation (SDE) is a deterministic differential equation with additional randomly varying term(s). This leads to a stochastic solution of the SDE as well. One important SDE is the Langevin equation

$$\frac{dx}{dt} = V(x) + \boldsymbol{\xi}(t) \quad (2.7)$$

with $V(x)$, the deterministic part and $\boldsymbol{\xi}(t)$, the stochastic part. The solution X_t of this equation is also another stochastic process.

2.3 *E-coli* Chemotaxis

Typical *Escherichia Coli* (*E-coli*) has a rod-like shape ($\sim 2\mu m$ long and of diameter $\sim 1\mu m$), having long flagella (typically spanning twice the length of the bacteria) distributed over its membrane [1, 14]. This micro-organism responds to external concentration gradients of some chemicals in its environment. The response can be negative; i.e moving down the gradient in case of chemical repellent gradient, or positive; i.e moving up the gradient in case of a chemical attractant gradient. The mechanism employed by this bacterium is to swim in near straight path (*run*) and periodically interrupt with a random re-orientation of its direction (*tumble*). This helps the bacterium to bias its movement to its preferred direction.

2.4 Scallop Theorem

Since the publication of Purcell's paper on the Life of low Reynolds number ($Re \ll 1$) [4], a physical principle underpinning swimming at low Reynolds number was brought to light. At this scale non-linear terms in Navier-Stokes equations vanishes and the equation becomes time reversible. Therefore, for any swimmer at this scale to propel itself (swim), it must undergo non-reciprocal deformations. This is known as Scallop Theorem. This lays the fundamental physical principle on which any man-made device operating at this conditions should satisfy. Though, for the *E-Coli* the directed motion (chemotaxis) comes from the *run-and-tumble* strategy due to the enormous thermal fluctuations in its environmental. Hence, in addition to swimmer satisfying the Scallop theorem, extra strategy is required to achieve directed motion (drift).

Navier - Stokes:

$$-\nabla p + \eta \nabla^2 \vec{v} = \cancel{\rho \frac{\partial \vec{v}}{\partial t}} + \rho \cancel{(\vec{v} \cdot \nabla) \vec{v}}$$

If $Q \ll 1$:

Time doesn't matter. The pattern of motion is the same, whether slow or fast, whether forward or backward in time.

The Scallop Theorem



Figure 6

Figure 2.1: Excerpt from Purcell's 1976 paper 'Life at low Reynolds number'

Chapter 3

2D Microswimmer Dynamics

In hydrodynamic environments, *E-coli* (a microswimmer) is subject to random fluctuations (thermal noise). Yet, it do sense chemoattractant gradient and move up the gradient despite the fluctuations. The bacteria accomplishes that by reducing its tumbling frequency (rate of random re-orientation) when moving in a favourable direction [1, 3]. This results in the cell's net drift velocity up the gradient. The thermal fluctuations occurs in much shorter time-scale than that of the *E-coli*.

Rotational frictional (viscous) drag on a microswimmer strongly depends on the swimmers geometrical shape and the axes to which it swims in case of swimmers with asymmetrical body shapes [14]. Consequently, when a swimmer changes its body geometry while swimming by some mechanism(s), the viscous drag on the swimmer changes as well. Thus, the helical structure of *E-coli* flagella comes in handy since when rotating in CCW mode, all the individual flagellum rotates in unison and forms a bundle (the swimmer will look like an ellipsoid moving lengthwise); while the flagella spread-out and rotates erratically in CW mode [1, 2, 14]. In other words, the bacteria enhances or reduces the effect of viscous drag acting on it just by changing its morphology. *E-coli* translational diffusion coefficient D is related to its rotational diffusion coefficient D_r as $D = v^2/6D_r$ [14, 15], where v is the

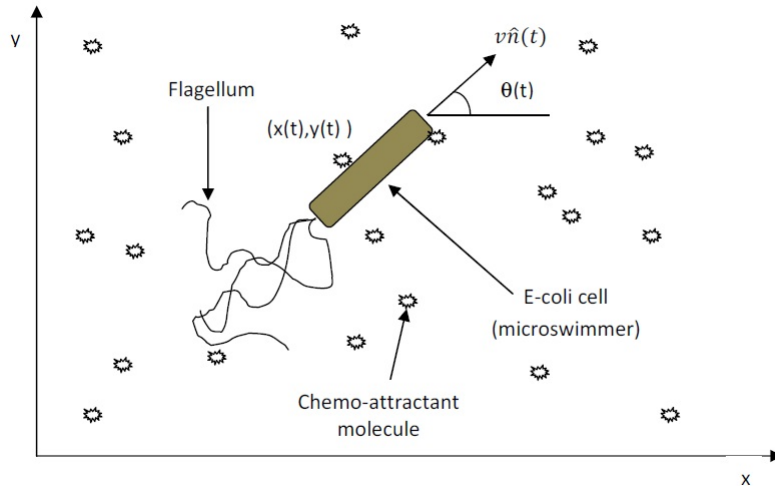


Figure 3.1: A schematic 2D *E-coli* (microswimmer) cell

average speed of the microswimmer. Roughly speaking, for a microswimmer with arbitrary shape, $D \propto v^2/D_r$ [14].

E-coli cell can be considered as a microswimmer that switches between two states; namely *run* (near straight swimming) and *tumble* (random re-orientation) states. The net motility behaviour of *E-coli* is largely dependent on the switching rates between these states. Switching between these states is totally random (probabilistic) in the absence of any gradient whereas in the presence of a concentration gradient, it varies over time depending on the gradient sensed. The cell's drift towards a chemoattractant (e.g fuel, food) source or away from chemorepellent (e.g medicine, poison) depends on how the swimmer periodically adjusts its transition rates upon temporal measurement of its environmental condition. Random telegraph process with *time dependent* transition rates fits perfectly to describe this switching process. What follows henceforth is the swimmer motility behaviour analysis, coupling the random telegraph process (RTP) to the swimmer associated Langevin equations.

3.1 The chemotaxis strategy

Firstly, it is important we introduce how random telegraph process demonstrates the swimmer chemotaxis strategy. *E-coli* alters its transition rate (also known as tumbling frequency) from *run* state to *tumble* state in response to environmental concentration gradient. The response modulates the transition rate around the mean adapted transition rate (i.e transition rate in the absence of a gradient). The transition rate [3,9,16] fitted to experimental data for moderate chemoattractant concentration intensity, $c(\mathbf{x}(t), t)$ reads

$$\omega(t) = \frac{1}{\tau_r} \left(1 - \int_{t-\tau}^t ds K(t-s) c(\mathbf{x}(s), s) \right) \quad (3.1)$$

where τ_r is the mean run-time in the absence of gradient, $K(t)$ is the response kernel, $c(\mathbf{x}(t), t)$ is the chemoattractant concentration profile in the environment, $\mathbf{x}(t)$ is the microswimmer trajectory (intrinsically stochastic) and τ is the characteristic response time ($\tau \sim 4$ seconds for *E-coli*) [1]. The linear dependence of $\omega(t)$ to the concentration field $c(\mathbf{x}(s), s)$ is due the assumption that the concentration gradient is weak and the principle of weak chemotactic response which requires that

$$\left| \int_{-\infty}^t ds K(t-s) c(\mathbf{x}(s), s) \right| \ll 1$$

We can therefore conveniently define the random telegraph process transition rates as

$$\lambda(t) = \lambda, \quad \mu(t) = \mu_0 \left(1 - \int_{t-\tau}^t ds K(t-s) c(\mathbf{x}(s), s) \right) \quad (3.2)$$

with μ_0 being the transition rate in the absence of concentration gradient and τ_r , $c(\mathbf{x}(t), t)$, $\mathbf{x}(t)$, τ retain their meanings from equation (3.1). The transition rate $\mu(t)$ depends on the history of the swimmer's past detections through the response term $\int_{t-\tau}^t ds K(t-s) c(\mathbf{x}(s), s)$. In the absence of chemotactic

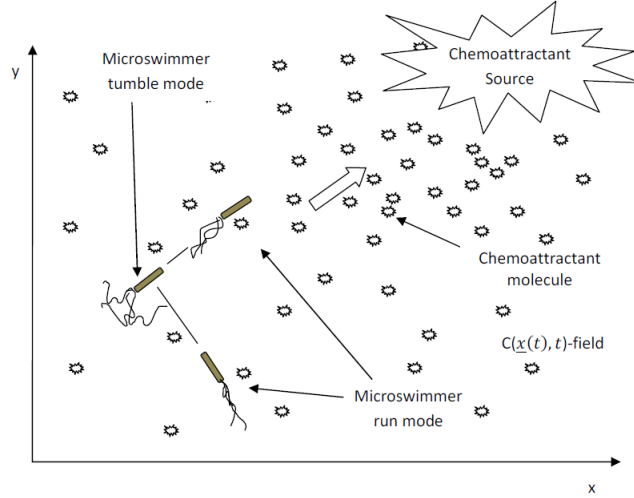


Figure 3.2: A 2D chemotactic *E-coli* (microswimmer) cell with a concentration gradient

strategy, the swimmer trajectory \mathbf{X}_t is purely diffusive - no drift; described by Brownian motion (Wiener process dB_t), such that $d\mathbf{X}(t) = \sqrt{2D}dB_t$. Where D is the swimmer translational diffusivity in an environment with no chemoattractant gradient.

The set of equations governing the transition dynamics (i.e the telegraph process) [11] reads

$$\partial_t P_1(t) = - \overbrace{\mu(t)P_1(t)}^{\text{loss}} + \overbrace{\lambda(t)P_2(t)}^{\text{gain}} \quad (3.3)$$

$$\partial_t P_2(t) = \underbrace{\mu(t)P_1(t)}_{\text{gain}} - \underbrace{\lambda(t)P_2(t)}_{\text{loss}} \quad (3.4)$$

$P_1(t) \equiv P(\alpha_1, t)$ and $P_2(t) \equiv P(\alpha_2, t)$ are probabilities of finding the swimmer with α_1 state variable and α_2 state variable at any time t respectively. $\mu(t)P_1(t)$ is the rate of probability loss (gain) due to transition from α_1 state to α_2 state and $\lambda(t)P_2(t)$ is the rate of probability gain (loss) due to transition

from α_2 state to α_1 state with the conditions

$$P_1(t) + P_2(t) = 1 \quad (3.5)$$

$$\text{and } P(\alpha, t_0 | \alpha_0, t_0) = \delta_{\alpha, \alpha_0} \quad (3.6)$$

We can choose to study different models using this process. One excellent possible choice of such models is that λ is a constant while $\mu(t)$ depends on the swimmer concentration detections history (\sim equivalent to the *E-coli* run-and-tumble chemotaxis strategy, equation 3.2). However, depending on the system one intends to study, we can as well choose $\lambda(t)$ to depend on the swimmer trajectory history in some field (e.g the concentration) while μ being a constant, or making both depend on the field detection history of interest; though, the field must be what the swimmer is sensitive to.

Now, from equation (3.3) and (3.5):

$$\begin{aligned} \partial_t P_1(t) &= -\lambda(t)P_1(t) + \mu(t)[1 - P_1(t)] \\ \partial_t P_1(t) + [\lambda(t) + \mu(t)]P_1(t) &= \mu(t) \end{aligned} \quad (3.7)$$

also from equation (3.4) and (3.5):

$$\begin{aligned} \partial_t P_2(t) &= +\lambda(t)[1 - P_2(t)] - \mu(t)P_2(t) \\ \partial_t P_2(t) + [\lambda(t) + \mu(t)]P_2(t) &= \lambda(t) \end{aligned} \quad (3.8)$$

Multiplying equation (3.7) by an integrating factor;

$$\Rightarrow \quad \partial_t \left\{ e^{\int_{t_0}^t dt' [\lambda(t') + \mu(t')]} P_1(t) \right\} = \mu(t) e^{\int_{t_0}^t dt' [\lambda(t') + \mu(t')]} \quad (3.9)$$

Integrating equation (3.9)

$$\int_{t_0}^t ds \quad \partial_s \left\{ e^{\int_{t_0}^s dt' [\lambda(t') + \mu(t')]} P_1(s) \right\} = \int_{t_0}^t ds \quad \mu(s) e^{\int_{t_0}^s dt' [\lambda(t') + \mu(t')]}$$

$$\left\{ e^{\int_{t_0}^s dt' [\lambda(t') + \mu(t')]} P_1(s) \right\}_{t_0}^t = \int_{t_0}^t ds \quad \mu(s) e^{\int_{t_0}^s dt' [\lambda(t') + \mu(t')]}$$

$$e^{\int_{t_0}^t dt' [\lambda(t') + \mu(t')]} P_1(t) - P_1(t_0) = \int_{t_0}^t ds \quad \mu(s) e^{\int_{t_0}^s dt' [\lambda(t') + \mu(t')]}$$

$$P_1(t) = e^{\int_{t_0}^t dt' [\lambda(t') + \mu(t')]} \left\{ \delta_{\alpha_1, \alpha_0} + \int_{t_0}^t ds \mu(s) e^{\int_{t_0}^s dt' [\lambda(t') + \mu(t')]} \right\}$$

Hence, the general solution is

$$P_1(t) = \delta_{\alpha_1, \alpha_0} e^{-\int_{t_0}^t dt' [\lambda(t') + \mu(t')]} + \int_{t_0}^t ds \quad \mu(s) e^{\int_t^s dt' [\lambda(t') + \mu(t')]} \quad (3.10)$$

Likewise for the $P_2(t)$, after repeating the calculations as above: we have from equation (3.8)

$$P_2(t) = \delta_{\alpha_2, \alpha_0} e^{-\int_{t_0}^t dt' [\lambda(t') + \mu(t')]} + \int_{t_0}^t ds \quad \lambda(s) e^{\int_t^s dt' [\lambda(t') + \mu(t')]} \quad (3.11)$$

The two equations (3.10 and 3.11) above describes the time evolution of the swimmer's chemotaxis process (or chemotactic strategy). Swimmer phase variables switching between the two phases in the Langevin equations that will follow are characterized by these two equations.

3.2 Associated Langevin Equations

In low Reynold's number ($\Re \ll 1$), inertial effects are negligible for a microswimmer [4]. A microswimmer stops as soon as the propulsive force ceases

- no coasting. Now, consider a microswimmer (e.g *E-coli* cell) moving in two dimensions (2D), with a net swimming speed $v(t)$, swimming along its unit director $\hat{\mathbf{n}}(t) = (\cos \theta(t), \sin \theta(t))$, where $\theta(t)$ is the orientation of the microswimmer to the x-axis at time t as illustrated in figure 3. The dynamics of this swimmer is represented by the Langevin stochastic differential equations below. *Runs* (CCW flagella rotation) corresponds to the microswimmer moving with near constant orientation θ interrupted by *tumbles* (CW flagella rotation) which are random re-orientation in same neighborhood \mathbf{x} that occur with transition rate $\mu(t)$. For all the analysis that follows, the swimmer hydrodynamic environment is assumed unbounded and stationary. Langevin equations [12] for this microswimmer coupled with the chemotaxis strategy (telegraph process) and expressing translational and rotational contributions separately are

$$\text{translational} \Rightarrow \quad \frac{d\mathbf{x}}{dt}(t) = v(t)\hat{\mathbf{n}}(t) + \boldsymbol{\xi}(t) \quad (3.12)$$

$$\text{rotational} \quad \Rightarrow \quad \frac{d\theta}{dt}(t) = \beta(t) \quad (3.13)$$

Explicitly, the equations coupling the different degrees of freedom are

$$\frac{dx}{dt}(t) = v(t) \cos \theta(t) + \gamma(t) \quad (3.14)$$

$$\frac{dy}{dt}(t) = v(t) \sin \theta(t) + \eta(t) \quad (3.15)$$

$$\frac{d\theta}{dt}(t) = \beta(t) \quad (3.16)$$

$\boldsymbol{\xi}(t) = (\gamma(t), \eta(t))$, $\beta(t)$ are stochastic Gaussian white noise processes whose autocorrelation functions are given by [17, 18]

$$\langle \boldsymbol{\xi}(t) \rangle = \mathbf{0}, \quad \langle \xi_i(t) \xi_j(s) \rangle = 2D \delta_{i,j} \delta(t-s) \quad (3.17)$$

$$\langle \beta(t) \rangle = 0, \quad \langle \beta(t) \beta(s) \rangle = 2D_r(t) \delta(t-s) \quad (3.18)$$

where D is the swimmer translational diffusion constant and $D_r(t)$ is the rotational diffusion coefficient.

Markov approximation of the above correlation functions is chosen as such because, the time scales of the molecular kicks that manifest as the random forces and torques acting on the swimmer are so small compared to the microswimmer's time scales and even much smaller than our macroscopic time scales. The fast state variables (rapidly varying variables) with respect to our macroscopic time scales are the Brownian randomization (thermal noise)- $\xi(t)$ and the random torque effect $\beta(t)$.

The two swimmer states (phases) described by the above Langevin equations (3.14,3.15, and 3.16) are:

run state (v_1, D_1): swimming state with high swimming velocity and low rotational diffusion.

tumble state (v_2, D_2): random re-orientation state with low swimming velocity and high rotational diffusion.

Therefore, the swimmer speed $v(t)$ and rotational diffusion coefficient $D_r(t)$ are characterized by the probabilities $P_1(t), P_2(t) = 1 - P_1(t)$ as follows:

$$v(t) = v_1 P_1(t) + v_2 P_2(t); \quad v_1 \gg v_2 \quad (3.19)$$

$$D_r(t) = D_1 P_1(t) + D_2 P_2(t); \quad D_1 \ll D_2 \quad (3.20)$$

Here, we assume that the time-scale of the switching rates μ, λ is much longer than the time-scale of the rotational diffusion $\sim D_r^{-1}$ of the swimmer. Recall our choice of the transition rates λ and $\mu(t)$ from equation (3.2), it require us calculating the integral

$$\int_{t-\tau}^t ds K(t-s) c(\mathbf{x}(s), s)$$

The kernel function $K(t)$ can in principle be taken to be any real continuous function in the interval $[0, \tau]$, such as $K(t) = \text{constant}$, or $K(t) = K_0 e^{-|t|/\tau}$.

Furthermore, the concentration $c(\mathbf{x}(t), t)$ can be Taylor expanded around t_0 as

$$\begin{aligned}
c(\mathbf{x}(t'), t') &= \sum_{l=0}^{\infty} \sum_{m=0}^{\infty} \frac{(\mathbf{x}(t') - \mathbf{x}(t_0))^l}{l!} \frac{(t' - t_0)^m}{m!} \frac{\partial^{l+m} c}{\partial \mathbf{x}^l \partial (t')^m}(\mathbf{x}(t_0), t_0) \\
&= c(\mathbf{x}(t_0), t_0) + (\mathbf{x}(t') - \mathbf{x}(t_0)) \cdot \nabla c(\mathbf{x}(t_0), t_0) + (t' - t_0) \partial_t c(\mathbf{x}(t_0), t_0) \\
&\quad + \frac{1}{2} ((\mathbf{x}(t') - \mathbf{x}(t_0)) \cdot \nabla)^2 c(\mathbf{x}(t_0), t_0) + \dots
\end{aligned} \tag{3.21}$$

At the swimmer micro-scale, the chemoattractant concentration $c(\mathbf{x}(t), t)$ varies very slowly in space and time. This is justified by the swimmer being of micron-scale size (*E-coli* has typical length of $\sim 2\mu m$ and $\sim 1\mu m$ diameter) [1]. Hence, this implies we can take the concentration $c(\mathbf{x}(t), t)$ a constant function of time $\partial_t c = 0$ (as viewed by the swimmer) and truncate the Taylor expansion of the concentration only to the quadratic order ($\nabla c, \nabla^2 c$ - which are also effectively constant to the swimmer). Concisely, we have

$$c(\mathbf{x}(t'), t') = c^0 + (\mathbf{x}(t') - \mathbf{x}(t_0)) \cdot \mathbf{c}^1 + (x_i(t') - x_i(t_0))(x_j(t') - x_j(t_0))c_{ij}^2 + \mathcal{O}(\nabla^3 c) \tag{3.22}$$

where the constant coefficients are

$$c^0 \equiv c(\mathbf{x}(t_0), t_0) \tag{3.23}$$

$$\mathbf{c}^1 \equiv \nabla c(\mathbf{x}(t_0), t_0) \tag{3.24}$$

$$c_{ij}^2 \equiv \frac{\partial^2}{\partial x_i \partial x_j} c(\mathbf{x}(t_0), t_0) \tag{3.25}$$

We note that since $\mu(t)$ is the transition rate from *run* state (state 1) to *tumble* state (state 2), to calculate the expression of $\mu(t)$, the swimmer has speed v_1 and rotational diffusion coefficient D_1 at this time t and due to the assumption we made on the separation of the time-scales above, one can

freely write

$$\mathbf{x}(t') - \mathbf{x}(t_0) = \int_{t_0}^{t'} dt_1 (v_1 \hat{\mathbf{n}}(t_1) + \boldsymbol{\xi}(t_1)) \quad (3.26)$$

$$\begin{aligned} (x_i(t') - x_i(t_0))(x_j(t') - x_j(t_0)) &= \int_{t_0}^{t'} dt_1 \int_{t_0}^{t'} dt_2 (v_1 \hat{n}_i(t_1) + \xi_i(t_1)) \\ &\quad \times (v_1 \hat{n}_j(t_2) + \xi_j(t_2)) \end{aligned} \quad (3.27)$$

Substituting equation (3.22) into equation (3.2) of the transition rate $\mu(t)$

$$\begin{aligned} \mu(t) &= \mu_0 \left(1 - \int_{t-\tau}^t ds K(t-s) c(\mathbf{x}(s), s) \right) \\ &= \mu_0 - \mu_0 \int_{t-\tau}^t dt' K(t-t') (c^0 + (\mathbf{x}(t') - \mathbf{x}(t_0)) \cdot \mathbf{c}^1 \\ &\quad + (x_i(t') - x_i(t_0))(x_j(t') - x_j(t_0))c_{ij}^2 + \mathcal{O}(\nabla^3 c)) \end{aligned} \quad (3.28)$$

Now we can write the transition rate in the form

$$\mu(t) = \mu_0 + \delta\mu + \mathcal{O}(\nabla^3 c); \quad \delta\mu = M_0(t)c^0 + \mathbf{M}_1(t) \cdot \mathbf{c}^1 + M_2^{ij}(t)c_{ij}^2 \quad (3.29)$$

where the time dependent coefficients are:

$$M_0(t) = -\mu_0 \int_{t-\tau}^t dt_1 K(t-t_1) \quad (3.30)$$

$$\mathbf{M}_1(t) = -\mu_0 \int_{t-\tau}^t dt_1 K(t-t_1) \int_{t_0}^{t_1} dt_2 (v_1 \hat{\mathbf{n}}(t_2) + \boldsymbol{\xi}(t_2)) \quad (3.31)$$

$$\begin{aligned} M_2^{ij}(t) &= -\frac{\mu_0}{2} \int_{t-\tau}^t dt_1 K(t-t_1) \int_{t_0}^{t_1} dt_2 \\ &\quad \times \int_{t_0}^{t_1} dt_3 (v_1 \hat{n}_i(t_2) + \xi_i(t_2))(v_1 \hat{n}_j(t_3) + \xi_j(t_3)) \end{aligned} \quad (3.32)$$

Therefore, we can now expand the expressions of the probabilities P_1 and P_2 (eqns 3.10,3.11) using the approximate expression of $\mu(t)$ (eqn. 3.29) keeping

only linear terms in $\delta\mu$ (i.e keeping only the linear terms in $c^0, \mathbf{c}^1, c_{ij}^2$)

$$P_1(t) = \bar{P}_1 + P_1^{(0)}c^0 + \mathbf{P}_1^{(1)}(t) \cdot \mathbf{c}^1 + P_1^{(2)ji}(t)c_{ij}^2 + \mathcal{O}(\nabla^3 c) \quad (3.33)$$

$$P_2(t) = \bar{P}_2 + P_2^{(0)}c^0 + \mathbf{P}_2^{(1)}(t) \cdot \mathbf{c}^1 + P_2^{(2)ji}(t)c_{ij}^2 + \mathcal{O}(\nabla^3 c) \quad (3.34)$$

where for the choice of the transitions rates: λ constant and $\mu(t)$ depends on the detections history for a chemotactic swimmer made in equation (3.2), we have

$$\bar{P}_1 = \frac{\mu_0}{\mu_0 + \lambda} \quad (3.35)$$

$$P_1^{(0)}(t) = \int_0^t ds (e^{(\mu_0+\lambda)(s-t)} - \delta_{\alpha_1, \alpha_0} e^{-(\mu_0+\lambda)t}) M_0(s) + \mu_0 \int_0^t ds e^{(\mu_0+\lambda)(s-t)} \int_t^s dt' M_0(t') \quad (3.36)$$

$$\mathbf{P}_1^{(1)}(t) = \int_0^t ds (e^{(\mu_0+\lambda)(s-t)} - \delta_{\alpha_1, \alpha_0} e^{-(\mu_0+\lambda)t}) \mathbf{M}_1(s) + \mu_0 \int_0^t ds e^{(\mu_0+\lambda)(s-t)} \int_t^s dt' \mathbf{M}_1(t') \quad (3.37)$$

$$P_1^{(2)ji}(t) = \int_0^t ds (e^{(\mu_0+\lambda)(s-t)} - \delta_{\alpha_1, \alpha_0} e^{-(\mu_0+\lambda)t}) M_2^{ji}(s) + \mu_0 \int_0^t ds e^{(\mu_0+\lambda)(s-t)} \int_t^s dt' M_2^{ji}(t') \quad (3.38)$$

similarly for $P_2(t) \equiv 1 - P_1(t)$, using equation (3.11) the coefficients can in the same manner (note that calculating one of the probabilities is enough for our calculations).

Then, substituting these judiciously approximate values into the transla-

tional Langevin equation of motion (3.12)

$$\begin{aligned}
\frac{d\mathbf{x}}{dt}(t) &= (v_1 P_1(t) + v_2 P_2(t)) \hat{\mathbf{n}}(t) + \boldsymbol{\xi}(t) \\
&= (v_1 \bar{P}_1 + v_2 \bar{P}_2) \hat{\mathbf{n}}(t) + \left[(v_1 \mathbf{P}_1^{(1)}(t) + v_2 \mathbf{P}_2^{(1)}(t)) \cdot \mathbf{c}^1 \right] \hat{\mathbf{n}}(t) \\
&\quad + (v_1 P_1^{(2)ji}(t) c_{ij}^2 + v_2 P_2^{(2)ji}(t) c_{ij}^2) \hat{\mathbf{n}}(t) + \boldsymbol{\xi}(t) \quad (3.39)
\end{aligned}$$

Consequently, averaging the translational Langevin equation (3.12) over the rotational fluctuations $\beta(t)$ and the telegraph process we get

$$\begin{aligned}
\frac{d\mathbf{x}}{dt} &= \left\langle \left[(v_1 \mathbf{P}_1^{(1)}(t) + v_2 \mathbf{P}_2^{(1)}(t)) \cdot \mathbf{c}^1 \right] \hat{\mathbf{n}}(t) \right\rangle_{\beta} \\
&\quad + \left\langle (v_1 P_1^{(2)ji}(t) c_{ij}^2 + v_2 P_2^{(2)ji}(t) c_{ij}^2) \hat{\mathbf{n}}(t) \right\rangle_{\beta} + \langle \boldsymbol{\xi}(t) \rangle_{\beta} \quad (3.40)
\end{aligned}$$

The first term can be simplified using triple product rule of vectors

$$(\mathbf{a} \cdot \mathbf{b})\mathbf{c} = (\mathbf{a} \cdot \mathbf{c})\mathbf{b} - \mathbf{a} \times (\mathbf{b} \times \mathbf{c})$$

such that

$$\begin{aligned}
\frac{d\mathbf{x}}{dt} &= \left\langle \left[v_1 \mathbf{P}_1^{(1)}(t) + v_2 \mathbf{P}_2^{(1)}(t) \right] \cdot \hat{\mathbf{n}}(t) \right\rangle_{\beta} \mathbf{c}^1 \\
&\quad + \left\langle \left[v_1 \mathbf{P}_1^{(1)}(t) + v_2 \mathbf{P}_2^{(1)}(t) \right] \times (\mathbf{c}^1 \times \hat{\mathbf{n}}(t)) \right\rangle_{\beta} \\
&\quad + \left\langle \left[v_1 P_1^{(2)ji}(t) c_{ij}^2 + v_2 P_2^{(2)ji}(t) c_{ij}^2 \right] \hat{\mathbf{n}}(t) \right\rangle_{\beta} + \boldsymbol{\xi}(t) \quad (3.41)
\end{aligned}$$

It can easily be seen that the second term

$$\left\langle \left[v_1 \mathbf{P}_1^{(1)}(t) + v_2 \mathbf{P}_2^{(1)}(t) \right] \times (\mathbf{c}^1 \times \hat{\mathbf{n}}(t)) \right\rangle_{\beta} = 0$$

Therefore, equation (3.41) reduces to

$$\frac{d\mathbf{x}}{dt} = \left\langle \left[v_1 \mathbf{P}_1^{(1)}(t) + v_2 \mathbf{P}_2^{(1)}(t) \right] \cdot \hat{\mathbf{n}}(t) \right\rangle_{\beta} \mathbf{c}^1 + \boldsymbol{\xi}_{new}(t) + \boldsymbol{\xi}(t) \quad (3.42)$$

Now written concisely,

$$\frac{d\mathbf{x}}{dt} = \mathbf{v}_{\text{eff}}(\mathbf{x}) + \boldsymbol{\xi}_{\text{eff}}(t) \quad (3.43)$$

where

$$\mathbf{v}_{\text{eff}}(\mathbf{x}) = \kappa \nabla c(\mathbf{x}); \quad \boldsymbol{\xi}_{\text{eff}}(t) = \boldsymbol{\xi}(t) + \boldsymbol{\xi}_{\text{new}} \quad (3.44)$$

and

$$\kappa = \left\langle \left[v_1 \mathbf{P}_1^{(1)}(t) + v_2 \mathbf{P}_2^{(1)}(t) \right] \cdot \hat{\mathbf{n}}(t) \right\rangle_{\beta} \quad (3.45)$$

$$\boldsymbol{\xi}_{\text{new}}(t) = \left\langle \left[v_1 P_1^{(2)ji}(t) c_{ij}^2 + v_2 P_2^{(2)ji}(t) c_{ij}^2 \right] \hat{\mathbf{n}}(t) \right\rangle_{\beta} \quad (3.46)$$

The parameter κ determines how effective the swimmer will chemotax in the presence of a gradient ∇c . It depends on the swimmer response function $K(t)$, the switching rates μ_0, λ , the fast and slow rotational diffusion constants D_2, D_1 as well as the fast and slow swimming speeds v_1, v_2 . We can notice some additional correlation term to the effective thermal fluctuations term $\boldsymbol{\xi}_{\text{new}}$ which comes from the complex rotational motion of the swimmer due to the chemotactic strategy and results in a net enhancement of the swimmer diffusivity (or mean square displacement, MSD).

Finally, given a particular form of the response kernel function $K(t)$, we can get explicit expressions of all state variables of interest.

3.3 Chemotaxis parameter κ and $\boldsymbol{\xi}_{\text{new}}$ noise

The expression of the chemotaxis parameter κ and $\boldsymbol{\xi}_{\text{new}}$ in the previous section are more intuitive for the model description, but tedious for specific swimmer calculations.

We can obtain similar results that contains only one of the probabilities and is much simpler to handle analytically.

From the Langevin equation (3.12) and the expressions $P_1(t) + P_2(t) = 1$;

$v(t) = v_1 P_1(t) + v_2 P_2(t)$ (eqn. 3.5 and eqn. 3.19 respectively), one can write

$$v(t) = (v_1 - v_2)P_1(t) + v_2$$

Also, we can re-write equation (3.39) as

$$\begin{aligned} \frac{d\mathbf{x}}{dt}(t) &= (v_1 - v_2)P_1(t)\hat{\mathbf{n}}(t) + v_2\hat{\mathbf{n}}(t) + \boldsymbol{\xi}(t) \\ &= (v_1 - v_2)\bar{P}_1 \hat{\mathbf{n}}(t) + \left[(v_1 - v_2)\mathbf{P}_1^{(1)}(t) \cdot \mathbf{c}^1 \right] \hat{\mathbf{n}}(t) \\ &\quad + (v_1 - v_2)P_1^{(2)ji}(t)c_{ij}^2 \hat{\mathbf{n}}(t) + v_2\hat{\mathbf{n}}(t) + \boldsymbol{\xi}(t) \end{aligned} \quad (3.47)$$

Averaging over the rotational fluctuations $\beta(t)$ and following same arguments as in the previous section, we get

$$\frac{d\mathbf{x}}{dt} = (v_1 - v_2) \left\langle \mathbf{P}_1^{(1)}(t) \cdot \hat{\mathbf{n}}(t) \right\rangle_{\beta} \mathbf{c}^1 + (v_1 - v_2) \left\langle P_1^{(2)ji}(t) \hat{\mathbf{n}}(t) \right\rangle_{\beta} c_{ij}^2 + \boldsymbol{\xi}(t) \quad (3.48)$$

where now κ is equivalently

$$\kappa = (v_1 - v_2) \left\langle \mathbf{P}_1^{(1)}(t) \cdot \hat{\mathbf{n}}(t) \right\rangle_{\beta}$$

and the additional noise

$$\boldsymbol{\xi}_{new}(t) = (v_1 - v_2) \left\langle P_1^{(2)ji}(t) \hat{\mathbf{n}}(t) \right\rangle_{\beta} c_{ij}^2$$

Now, from the expressions of $\bar{P}_1, P_1^{(0)}, \mathbf{P}_1^{(1)}$ and $P_1^{(2)ji}$ (eqns. 3.35 to 3.38)

$$\begin{aligned} \left\langle \bar{P}_1 \hat{\mathbf{n}}(t) \right\rangle_{\beta} &= \frac{\mu_0}{\mu_0 + \lambda} \left\langle \hat{\mathbf{n}}(t) \right\rangle_{\beta} \quad (3.49) \\ \left\langle P_1^{(0)}(t) \hat{\mathbf{n}}(t) \right\rangle_{\beta} &= \left\langle \hat{\mathbf{n}}(t) \right\rangle_{\beta} \int_0^t ds \left(e^{(\mu_0 + \lambda)(s-t)} - \delta_{\alpha_1, \alpha_0} e^{-(\mu_0 + \lambda)t} \right) M_0(s) \\ &\quad + \mu_0 \left\langle \hat{\mathbf{n}}(t) \right\rangle_{\beta} \int_0^t ds e^{(\mu_0 + \lambda)(s-t)} \int_t^s dt' M_0(t') \end{aligned} \quad (3.50)$$

$$\begin{aligned} \langle \mathbf{P}_1^{(1)}(t) \cdot \hat{\mathbf{n}}(t) \rangle_\beta &= \int_0^t ds \left(e^{(\mu_0+\lambda)(s-t)} - \delta_{\alpha_1, \alpha_0} e^{-(\mu_0+\lambda)t} \right) \langle \mathbf{M}_1(s) \cdot \hat{\mathbf{n}}(t) \rangle_\beta \\ &\quad + \mu_0 \int_0^t ds e^{(\mu_0+\lambda)(s-t)} \int_t^s dt' \langle \mathbf{M}_1(t') \cdot \hat{\mathbf{n}}(t) \rangle_\beta \end{aligned} \quad (3.51)$$

$$\begin{aligned} \langle P_1^{(2)ji}(t) \hat{\mathbf{n}}(t) \rangle_\beta &= \int_0^t ds \left(e^{(\mu_0+\lambda)(s-t)} - \delta_{\alpha_1, \alpha_0} e^{-(\mu_0+\lambda)t} \right) \langle M_2^{ji}(s) \hat{\mathbf{n}}(t) \rangle_\beta \\ &\quad + \mu_0 \int_0^t ds e^{(\mu_0+\lambda)(s-t)} \int_t^s dt' \langle M_2^{ji}(t') \hat{\mathbf{n}}(t) \rangle_\beta \end{aligned} \quad (3.52)$$

Therefore, using eqns (3.31,3.32) and the correlation $\langle \hat{n}_i(t) \hat{n}_j(s) \rangle = \frac{1}{2} \delta_{ij} e^{-\int_s^t D_r(t') dt'}$

$$\begin{aligned} \langle \mathbf{M}_1(s) \cdot \hat{\mathbf{n}}(t) \rangle_\beta &= -\mu_0 \int_{s-\tau}^s dt_1 K(s-t_1) \\ &\quad \times \int_{t_0}^{t_1} dt_2 \left(v_1 \langle \hat{\mathbf{n}}(t_2) \cdot \hat{\mathbf{n}}(t) \rangle_\beta + \boldsymbol{\xi}(t_2) \langle \hat{\mathbf{n}}(t) \rangle_\beta \right) \\ &= -\mu_0 v_1 \int_{s-\tau}^s dt_1 K(s-t_1) \int_{t_0}^{t_1} dt_2 e^{-D_1(t-t_2)} \\ &= -\frac{\mu_0 v_1}{D_1} \int_{s-\tau}^s dt_1 K(s-t_1) \left(e^{-D_1(t-t_1)} - e^{-D_1(t-t_0)} \right) \end{aligned} \quad (3.53)$$

Taking the Taylor expansion of the concentration profile (eqn. 3.22) to be around the swimmer current vicinity or simply $t_0 = t$, we have

$$\langle \mathbf{M}_1(s) \cdot \hat{\mathbf{n}}(t) \rangle_\beta = \frac{\mu_0 v_1}{D_1} \int_{s-\tau}^s dt_1 K(s-t_1) \left(1 - e^{-D_1(t-t_1)} \right) \quad (3.54)$$

and the noise

$$\begin{aligned}
\langle M_2^{ij}(s)\hat{\mathbf{n}}(t)\rangle_\beta &= -\frac{\mu_0 v_1}{2} \int_{s-\tau}^s dt_1 K(s-t_1) \int_{t_0}^{t_1} dt_2 \\
&\quad \times \int_{t_0}^{t_1} dt_3 (e^{-D_1(t-t_2)} \xi_j(t_3), e^{-D_1(t-t_3)} \xi_i(t_2)) \\
&= -\frac{\mu_0 v_1}{2} \int_{s-\tau}^s dt_1 K(s-t_1) \\
&\quad \times \int_{t_0}^{t_1} dt' e^{-D_1(t-t')} \left(\int_{t_0}^{t_1} dt_3 \xi_j(t_3), \int_{t_0}^{t_1} dt_2 \xi_i(t_2) \right) \\
&= -\frac{\mu_0 v_1}{2} \int_{s-\tau}^s dt_1 K(s-t_1) \\
&\quad \times \int_{t_0}^{t_1} dt' e^{-D_1(t-t')} (W(t_1) - W(t_0), W(t_1) - W(t_0)) \\
&= -\frac{\mu_0 v_1}{2} \int_{s-\tau}^s dt_1 K(s-t_1) \\
&\quad \times \int_{t_0}^{t_1} dt' e^{-D_1(t-t')} (W(t_1) - W(t_0)) \hat{\boldsymbol{\xi}}_{new} \tag{3.55}
\end{aligned}$$

with

$$\int_{t_0}^{t_1} ds \xi_j(s) = \int_{t_0}^{t_1} dW_s = W(t_1) - W(t_0)$$

a wiener process [11] and $\hat{\boldsymbol{\xi}}_{new}$ a unit vector. This shows that

$$\langle M_2^{ij}(s)\hat{\mathbf{n}}(t)\rangle_{\beta, W_s} = 0; \quad \Rightarrow \quad \langle \hat{\boldsymbol{\xi}}_{new}(t)\rangle_{\beta, W_s} = 0 \tag{3.56}$$

Equation (3.55) indicates that the term $\boldsymbol{\xi}_{new}$ is a fluctuating function (noise) with zero mean and represents the enhanced diffusion of the swimmer due to the complex correlations from the chemotactic strategy as noted earlier.

We can now conveniently look at some swimmer specific examples.

I. Swimmer with $K(t) = K_0$ (constant)

A swimmer with constant response kernel will have

$$\begin{aligned}
\langle \mathbf{M}_1(s) \cdot \hat{\mathbf{n}}(t) \rangle_\beta &= -\frac{\mu_0 v_1}{D_1} \int_{s-\tau}^s dt_1 K(s-t_1) (e^{-D_1(t-t_1)} - e^{-D_1(t-t_0)}) \\
&= -\frac{\mu_0 v_1 K_0}{D_1} \int_{s-\tau}^s dt_1 (e^{-D_1(t-t_1)} - e^{-D_1(t-t_0)}) \\
&= \frac{\mu_0 v_1 K_0}{D_1} \tau e^{-D_1(t-t_0)} - \frac{\mu_0 v_1 K_0 (1 - e^{-D_1 \tau})}{D_1^2} e^{-D_1(t-s)} \\
&= A + B e^{-D_1(t-s)} \tag{3.57}
\end{aligned}$$

where

$$A = \frac{\mu_0 v_1 K_0}{D_1} \tau; \quad B = -\frac{\mu_0 v_1 K_0 (1 - e^{-D_1 \tau})}{D_1^2}$$

Now, assuming $\alpha_0 = \alpha_2$ (it does not matter which state the swimmer starts with since the term(s) involving $\delta_{\alpha, \alpha_0}$ decays rapidly with time)

$$\begin{aligned}
\langle \mathbf{P}_1^{(1)}(t) \cdot \hat{\mathbf{n}}(t) \rangle_\beta &= \int_0^t ds e^{(\mu_0 + \lambda)(s-t)} (A + B e^{-D_1(t-s)}) \\
&\quad + \mu_0 \int_0^t ds e^{(\mu_0 + \lambda)(s-t)} \int_t^s dt' (A + B e^{-D_1(t-t')}) \\
&= \frac{A (1 - e^{-(\mu_0 + \lambda)t})}{(\mu_0 + \lambda)} + \frac{B (1 - e^{-(\mu_0 + \lambda + D_1)t})}{(\mu_0 + \lambda + D_1)} \\
&\quad - \frac{\mu_0 A t (e^{-(\mu_0 + \lambda)t})}{(\mu_0 + \lambda)} - \frac{\mu_0 A (1 - e^{-(\mu_0 + \lambda)t})}{(\mu_0 + \lambda)^2} \\
&\quad + \frac{\mu_0 B (1 - e^{-(\mu_0 + \lambda + D_1)t})}{D_1 (\mu_0 + \lambda + D_1)} - \frac{\mu_0 B (1 - e^{-(\mu_0 + \lambda)t})}{D_1 (\mu_0 + \lambda)} \tag{3.58}
\end{aligned}$$

In which the limiting expression of $\langle \mathbf{P}_1^{(1)}(t) \cdot \hat{\mathbf{n}}(t) \rangle_\beta$ for $t \gg 1/\mu, 1/\lambda$ is

$$\begin{aligned} \langle \mathbf{P}_1^{(1)}(t) \cdot \hat{\mathbf{n}}(t) \rangle_\beta &\simeq \frac{A}{(\mu_0 + \lambda)} + \frac{B}{(\mu_0 + \lambda + D_1)} - \frac{\mu_0 A}{(\mu_0 + \lambda)^2} \\ &\quad + \frac{\mu_0 B}{D_1(\mu_0 + \lambda + D_1)} - \frac{\mu_0 B}{D_1(\mu_0 + \lambda)} \\ &= \frac{\mu_0 \lambda v_1 K_0 \tau}{D_1(\mu_0 + \lambda)^2} \left[1 - \frac{(1 - e^{-D_1 \tau})(\mu_0 + \lambda)}{\tau D_1(\mu_0 + \lambda + D_1)} \right] \end{aligned} \quad (3.59)$$

Hence

$$\kappa \simeq (v_1 - v_2) \frac{\mu_0 \lambda v_1 K_0 \tau}{D_1(\mu_0 + \lambda)^2} \left[1 - \frac{(1 - e^{-D_1 \tau})(\mu_0 + \lambda)}{\tau D_1(\mu_0 + \lambda + D_1)} \right] \quad (3.60)$$

II. Swimmer with $K(t) = K_0 e^{-|t|L}$ (K_0, L are constants)

Similarly for a swimmer with an exponential kernel, we will have

$$\begin{aligned} \langle \mathbf{M}_1(s) \cdot \hat{\mathbf{n}}(t) \rangle_\beta &= \frac{\mu_0 v_1}{D_1} \int_{s-\tau}^s dt_1 K(s-t_1) (1 - e^{-D_1(t-t_1)}) \\ &= \frac{\mu_0 v_1 K_0}{D_1} \int_{s-\tau}^s dt_1 e^{-(s-t_1)L} (1 - e^{-D_1(t-t_1)}) \\ &= \frac{\mu_0 v_1 K_0 (1 - e^{-L\tau})}{D_1 L} - \frac{\mu_0 v_1 K_0 (1 - e^{-(D_1+L)\tau})}{D_1 (D_1 + L)} e^{-D_1(t-s)} \\ &= A + B e^{-D_1(t-s)} \end{aligned} \quad (3.61)$$

where

$$A = \frac{\mu_0 v_1 K_0 (1 - e^{-L\tau})}{D_1 L}; \quad B = -\frac{\mu_0 v_1 K_0 (1 - e^{-(D_1+L)\tau})}{D_1 (D_1 + L)}$$

Therefore,

$$\begin{aligned}
\left\langle \mathbf{P}_1^{(1)}(t) \cdot \hat{\mathbf{n}}(t) \right\rangle_\beta &= \int_0^t ds e^{(\mu_0+\lambda)(s-t)} (A + B e^{-D_1(t-s)}) \\
&\quad + \mu_0 \int_0^t ds e^{(\mu_0+\lambda)(s-t)} \int_t^s dt' (A + B e^{-D_1(t-t')}) \\
&= \frac{A(1 - e^{-(\mu_0+\lambda)t})}{(\mu_0 + \lambda)} + \frac{B(1 - e^{-(\mu_0+\lambda+D_1)t})}{(\mu_0 + \lambda + D_1)} \\
&\quad - \frac{\mu_0 A t (e^{-(\mu_0+\lambda)t})}{(\mu_0 + \lambda)} - \frac{\mu_0 A (1 - e^{-(\mu_0+\lambda)t})}{(\mu_0 + \lambda)^2} \\
&\quad + \frac{\mu_0 B (1 - e^{-(\mu_0+\lambda+D_1)t})}{D_1(\mu_0 + \lambda + D_1)} - \frac{\mu_0 B (1 - e^{-(\mu_0+\lambda)t})}{D_1(\mu_0 + \lambda)} \quad (3.62)
\end{aligned}$$

For our macroscopic long time $t \gg 1/\mu, 1/\lambda$

$$\begin{aligned}
\left\langle \mathbf{P}_1^{(1)}(t) \cdot \hat{\mathbf{n}}(t) \right\rangle_\beta &\simeq \frac{A}{(\mu_0 + \lambda)} + \frac{B}{(\mu_0 + \lambda + D_1)} - \frac{\mu_0 A}{(\mu_0 + \lambda)^2} \\
&\quad + \frac{\mu_0 B}{D_1(\mu_0 + \lambda + D_1)} - \frac{\mu_0 B}{D_1(\mu_0 + \lambda)} \\
&= \frac{\mu_0 \lambda v_1 K_0 (1 - e^{-L\tau})}{D_1 L (\mu_0 + \lambda)^2} \left[1 - \frac{(1 - e^{-(D_1+L)\tau})(\mu_0 + \lambda)L}{(1 - e^{-L\tau})(\mu_0 + \lambda + D_1)(D_1 + L)} \right] \quad (3.63)
\end{aligned}$$

Now, it follows that

$$\kappa \simeq (v_1 - v_2) \frac{\mu_0 \lambda v_1 K_0 (1 - e^{-L\tau})}{D_1 L (\mu_0 + \lambda)^2} \left[1 - \frac{(1 - e^{-(D_1+L)\tau})(\mu_0 + \lambda)L}{(1 - e^{-L\tau})(\mu_0 + \lambda + D_1)(D_1 + L)} \right] \quad (3.64)$$

Chapter 4

Discussion

So far, we have successfully coupled the random telegraph process (representing chemotaxis strategy) to the swimmer associated Langevin equation. We were able to obtain an explicit expression of the chemotaxis parameter κ for a given microswimmer characterized by chemotactic response function, $K(t)$, *run*, (v_1, D_1) , and *tumble* phases with switching rates (μ, λ) , in the presence of concentration profile $c(\mathbf{x}(t), t)$. It is shown that the swimmer actually drifts in the presence of a concentration gradient ∇c and the swimmer drift velocity is limited by its characteristics. This highlights the dependence of swimmer's chemotaxis efficiency to its physical traits (such as the swimming speeds v_1, v_2 and rotational diffusion constant D_1).

This model could be a step more towards the right paradigm for designing a two-state artificial microswimmer.

Part of the goals of this thesis originally includes obtaining swimmer mean square angular deviation (MSAD) and mean square displacement (MSD) for different possible swimmer response functions. But, due to time constraint, this is only partially achieved. However, using the expressions of the chemotaxis parameter κ and the effective Langevin equation, One can easily calculate any quantity of interest (e.g MSAD, MSD, drift velocity v_d). For example, in Appendix I below, it is shown how this could be done in prin-

ciple (i.e generic procedure). In addition, to illustrate a simple scenario, a simple swimmer in a homogeneous concentration profile ($\nabla c = 0$) MSAD and MSD were obtained.

In case of swimmer population, additional interaction terms may significantly affect the chemotaxis parameter. Also, detail numerical simulations of this model may open up new investigation paradigms.

APPENDICES

A: Mean-Squared Angular Deviation (MSAD)

MSAD estimates the precision to which a swimmer swims along a straight path. It gives the average deviation to the deterministic swimming direction. Integrating equation (3.16), one gets

$$\theta(t) - \theta(0) = \int_0^t dt' \beta(t') \quad (4.1)$$

and the rotational diffusion coefficient

$$D_r(t) = D_1 P_1(t) + D_2 P_2(t)$$

Squaring the integral in equation (4.1) and averaging over the random processes (random torques, the telegraph process and all possible trajectories),

$$\begin{aligned} \langle \Delta\theta^2(t) \rangle &= \int_0^t dt_1 \int_0^t dt_2 \langle \beta(t_1) \beta(t_2) \rangle \\ &= \int_0^t dt_1 \int_0^t dt_2 2D_r(t_2) \delta(t_2 - t_1) \\ &= 2 \int_0^t dt_1 D_r(t_1) \end{aligned} \quad (4.2)$$

substituting the expression for the rotational diffusion coefficient $D_r(t)$ equation (??),

$$\begin{aligned}
\langle \Delta \theta^2(t) \rangle &= 2 \int_0^t dt_1 [D_2 - (D_2 - D_1)P_1(t_1)] \\
&= \left(\frac{\lambda D_1 + \mu_0 D_2}{\lambda + \mu_0} \right) t - 2(D_2 - D_1) \int_0^t dt_1 \langle P_1^{(0)} c^0 \rangle \\
&\quad - 2(D_2 - D_1) \int_0^t dt_1 \langle \mathbf{P}_1^{(1)}(t_1) \cdot \mathbf{c}^1 \rangle - 2(D_2 - D_1) \int_0^t dt_1 \langle P_1^{(2)ji}(t_1) c_{ij}^2 \rangle
\end{aligned} \tag{4.3}$$

We can easily notice the different contributions from the swimmer intrinsic properties $v_{1,2}, K(t), D_{1,2}$ and the external (environmental conditions) to the average mean deviation of the swimming direction. The first term is the mean deviation of a non-chemotactic swimmer irrespective of the environmental conditions, since for this swimmer $K(t) = 0$ and therefore the deviation remains always constant. The second term is the contribution that comes from the nature of the swimmer's response kernel $K(t)$. While the third and the fourth terms comes from the nature of the concentration gradient present in the swimmer environment.

B: Mean-Squared Displacement (MSD)

This is the average displacement or translational diffusion displacement of a swimmer undergoing random walk motion (here *runs* and *tumbles*). Starting with the swimmer trajectory (i.e integrating equations 3.14,3.15)

$$x(t) - x(0) = \int_0^t v(t) \cos \theta(t_1) dt_1 + \int_0^t \xi(t_1) dt_1 \tag{4.4}$$

$$y(t) - y(0) = \int_0^t v(t) \sin \theta(t_1) dt_1 + \int_0^t \eta(t_1) dt_1 \tag{4.5}$$

In which the (chemotactic) swimmer extract a net propulsion with an

average displacement components

$$\langle \Delta x(t) \rangle = \int_0^t \langle v(t) \cos \theta(t_1) \rangle dt_1 \quad (4.6)$$

$$\langle \Delta y(t) \rangle = \int_0^t \langle v(t) \sin \theta(t_1) \rangle dt_1 \quad (4.7)$$

where the angle brackets $\langle \dots \rangle$ denotes averaging over all the fast variables including the all possible trajectories X_t .

Hence, the swimmer have an average drift velocity (average speed a swimmer swim up a concentration gradient) up a chemoattractant gradient. The drift velocity can be obtained from the effective Langevin equation (3.43) by averaging over the translational thermal noise $\xi(t)$ and all possible trajectories.

$$\begin{aligned} \left\langle \frac{d\mathbf{x}}{dt} \right\rangle &= \langle \mathbf{v}_{\text{eff}}(\mathbf{x}) \rangle + \langle \xi_{\text{eff}}(t) \rangle \\ \Rightarrow v_d &= \kappa \nabla c(\mathbf{x}) \end{aligned} \quad (4.8)$$

However, for a mutant swimmer undergoing *runs* and *tumbles* without a strategy (directional bias) $v(t) = \bar{v} = v_1 \bar{P}_1 + v_2 \bar{P}_2$

$$(\bar{v} \langle \cos \theta(t_1) \rangle, \bar{v} \langle \sin \theta(t_1) \rangle) = 0 \quad \Rightarrow \quad v_d = 0$$

while for a swimmer with chemotactic strategy in the presence of a gradient, generally,

$$(\langle v(t) \cos \theta(t_1) \rangle, \langle v(t) \sin \theta(t_1) \rangle) \neq 0 \quad \Rightarrow \quad v_d = \kappa \nabla c(\mathbf{x})$$

Another quantity of interest is the swimmer effective diffusivity, which is related to MSD through the fluctuation-dissipation relation [1, 14]. Therefore, to get the MSD, one need to square and eliminate the fast variables (averaging

over the fast variables) in the effective Langevin equation (3.43):

$$\begin{aligned}
\langle \Delta L^2(t) \rangle &= \langle \Delta x^2(t) \rangle + \langle \Delta y^2(t) \rangle \\
&= \int_0^t dt_1 \int_0^{t_1} dt_2 (\kappa \nabla c(\mathbf{x}(t_1)) + \boldsymbol{\xi}_{\text{eff}}) \cdot (\kappa \nabla c(\mathbf{x}(t_2)) + \boldsymbol{\xi}_{\text{eff}}) \\
&= (4D + |\boldsymbol{\xi}_{\text{new}}|^2)t + \kappa^2 \int_0^t dt_1 \int_0^{t_1} dt_2 \nabla c(\mathbf{x}(t_1)) \cdot \nabla c(\mathbf{x}(t_2)) \quad (4.9)
\end{aligned}$$

Lets analyze the dynamics for a simple swimmer environmental condition (with constant response function, $K(t) = \text{constant}$).

Homogeneous (constant) concentration profile

$$c(\mathbf{x}, t) = c^0$$

From the expression of mean rotational coefficient (??), it simplifies to

$$\langle D_r(t) \rangle = D_1 + (D_2 - D_1) (\bar{P}_1 + P_1^{(0)}(t)) c^0 \quad (4.10)$$

while the *mean squared angular deviation (MSAD)*

$$\langle \Delta \theta^2(t) \rangle = D_1 t + (D_2 - D_1) \int_0^t dt_1 \left(\bar{P}_1 + P_1^{(0)}(t_1) \right) c^0 \quad (4.11)$$

with limiting behaviours

$$\langle \Delta \theta^2(t) \rangle \approx \begin{cases} (D_1 + D_2)t - \left(\frac{\lambda D_1 + \mu_0 D_2}{\lambda + \mu_0} \right) & t \gg 1/\mu_0, 1/\lambda \\ 2D_1 t + (\lambda D_1 - \mu_0 D_2)t^2 & t \ll 1/\mu_0, 1/\lambda. \end{cases} \quad (4.12)$$

and the *mean squared displacement* (MSD)

$$\begin{aligned}
\langle \Delta L^2(t) \rangle &= \langle \Delta x^2(t) \rangle + \langle \Delta y^2(t) \rangle \\
&= \int_0^t dt_1 \int_0^t dt_2 (\kappa \nabla c(\mathbf{x}(t_1)) + \boldsymbol{\xi}_{\text{eff}}) \cdot (\kappa \nabla c(\mathbf{x}(t_2)) + \boldsymbol{\xi}_{\text{eff}}) \\
&= 4Dt + |\boldsymbol{\xi}_{\text{new}}|^2 t + \kappa^2 \int_0^t dt_1 \int_0^t dt_2 \nabla c(\mathbf{x}(t_1)) \cdot \nabla c(\mathbf{x}(t_2)) \quad (4.13)
\end{aligned}$$

which simplifies to

$$\Delta L^2(t) = 4Dt \quad (4.14)$$

since $|\boldsymbol{\xi}_{\text{new}}|^2$ is a function c_{ij}^2 - second derivative of the concentration field.

Appendix II

Unit Director Auto-correlation Function

For a Gaussian noise $\beta(t)$, the distribution functional is [17]

$$P[\beta(t)] = \frac{1}{Z} \exp\left(-\int dt' \frac{\beta^2(t')}{4}\right) \quad (4.15)$$

$$\text{with } Z = \int \mathcal{D}\beta(t') \exp\left(-\int dt' \frac{\beta^2(t')}{4}\right) \quad \text{and } \mathcal{D}\beta(t) \equiv \prod_t d\beta(t) \quad (4.16)$$

The unit director autocorrelation function $\langle \hat{\mathbf{n}}(t_1) \cdot \hat{\mathbf{n}}(t_2) \rangle$ goes

$$\begin{aligned} \langle \hat{\mathbf{n}}(t_1) \cdot \hat{\mathbf{n}}(t_2) \rangle &= \int \frac{\mathcal{D}\beta(t')}{Z} \exp\left[-\int dt' \frac{\beta(t')^2}{4} \mp i \int_{t_1}^{t_2} dt' \sqrt{D_r(t')} \beta(t')\right] \\ &= \int \frac{\mathcal{D}\beta(t')}{Z} \exp\left[-\int_{t_1}^{t_2} dt' \left(\frac{\beta(t')^2}{4} \pm i \sqrt{D_r(t')} \beta(t')\right)\right] \end{aligned}$$

completing the square:

$$\begin{aligned} \langle \hat{\mathbf{n}}(t_1) \cdot \hat{\mathbf{n}}(t_2) \rangle &= \int \frac{\mathcal{D}\beta(t')}{Z} \exp\left(-\int_{t_1}^{t_2} dt' \frac{\beta(t')^2 \pm i4\sqrt{D_r(t')} \beta(t')}{4}\right) \\ &= \int \frac{\mathcal{D}\beta(t')}{Z} \exp\left[-\int_{t_1}^{t_2} dt' \left(\frac{(\beta(t') \pm i2\sqrt{D_r(t')})^2}{4} + D_r(t')\right)\right] \end{aligned}$$

$$\begin{aligned}
\langle \hat{\mathbf{n}}(t_1) \cdot \hat{\mathbf{n}}(t_2) \rangle &= e^{-\int_{t_1}^{t_2} dt' D_r(t')} \int \frac{\mathcal{D}\beta(t')}{Z} \exp\left(-\int_{t_1}^{t_2} dt' \frac{(\beta(t') \pm i2D_r(t'))^2}{4}\right) \\
&= \exp\left(-\int_{t_1}^{t_2} dt' D_r(t')\right)
\end{aligned}$$

Therefore,

$$\left\langle e^{\pm i \int_{t_1}^{t_2} dt' \beta(t')} \right\rangle = e^{-\int_{t_1}^{t_2} dt' D_r(t')} \quad (4.17)$$

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