School of Physics and Astronomy

Proposed Project Title
First Year Report and Literature Review

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Abstract

The abstract is a short concise outline of your project area, **of no more than 100 words**.

Signature: Date:

Supervisor: Dr. Rosalind Allen

Contents

1 Background

Since their discovery in the early 1900s [1], antibiotics have shaped modern medicine, and indeed modern society as a whole. Yet despite their prevalence, with over 260,000,000 courses of antibiotics prescribed in the USA alone each year [2], very little is still known about the actual underlying pharmacodynamics. I.e., how these chemicals actually regulate the growth and death of bacteria. This lack of understanding is becoming increasingly significant with the rising emergence of antibiotic resistance. There were over 58,000 deaths in newborns under the age of a year in India in 2013 due to drug-resistant strains of bacteria [3], with experts predicting that the number of deaths from antibiotic-resistant bacteria will number in the millions by 2050 [4].

This project aims to shed further light on how the application of antibiotics causes bacterial populations to evolve and proliferate over time. In particular, in the cases of when the applied antibiotic concentration has the form of a gradient. A considerable portion of antibiotic research has been performed under ideal conditions with constant, uniform antibiotic concentration [5], however it has only recently been proposed that the effects of spatial heterogeneity may be a major factor in the emergence of resistance and the efficacy of drugs [6]. While these concentration gradients can simply arise due to scenarios such as diffusion throughout body tissue [7], the scenario which is most pertinent to this project is that of antibiotic concentration throughout biofilms.

Biofilms arise when microbial organisms adhere irreversibly to a surface and then begin to secrete various polymers which further aid in surface and inter-microbial attachment [8] and creates a "slimey" surface. These structures are particularly problematic as it is difficult to achieve sufficient drug penetration to adequately curtail microbial growth, which leads to an increase in the persistence of infections [9].

The ability to inhibit and even prevent biofilm growth and formation has not only a multitude of medical applications, but industrial as well. In the shipping industry it's estimated that around 10%, up to even 45%, of all fuel consumption of large shipping vessels arises from overcoming the hydrodynamic drag caused by biofilm formation on ship hulls below the water level [10]. This not only has economic influences, but also major environmental implications. When compared to other nations, the shipping industry is the 7th largest producer of CO_2 on the planet [11]. Therefore, research into how these marine biofilms form and develop is incredibly important.

Recently, several physical methods of reducing marine biofouling have been developed, which range from physical coatings that inhibit microbial attachment due to their topography [12] to usage of ultraviolet radiation [13]. However, the most widespread technique is that of anti-microbial paints which are applied to the boat hulls and then leach various antimicrobial compounds over time which inhibit biofouling [14]. It is this latter method which is of relevant interest to this project due to its analogous nature of applying antibiotics to bacterial biofilms.

This project will involve creating simulations of a range of scenarios where bacterial populations experience antibiotic gradients, and will investigate how these populations develop over time. Including but not limited to; the effects of bacterial evolution, differing types of growth-rate dependent antibiotics and populations with heterogeneous species and resistance distributions.

2 Review of Background Bibliography

- Causes of antibiotic crisis
- growth rate dependent antibiotics, β-lactams etc
- mention the differnt algorithms possible for the sims, gillespie etc - and give overview of what we used
- overview of biofouling, current ship hull anti-microbes
- difference of films and fouls
- surface colonisation
- opposite gradient directions for films and fouls
- how biocidal paint works, diffusion coefficients etc

The main articles used at this point in the project is [15] and [16]

In this section detail the main supporting references and articles [**?**] for your intended area of research and, most importantly, your critical evaluation of their relevance. Also where your subject draws from multiple disciplines, do not forget to include key reference from each discipline, even if they are relatively old [**?**].

This is the main part of your review and is the part that will be of use to you when preparing for your thesis. Here try and identify as many of the key references as possible, and enter then into a `BibTeX` file that you will use later. Remember that recording the page number, titles and details of these key articles *now* will save you hours of searching through *Web-of-Knowledge* the day before your submit your thesis!

This part should be written in standard scientific language, aimed at the *experts in the field*. This is the main part of your first year report, and is expected to be 10 pages in length.

3 Progress to Date

Progress made so far in this project can be organised into several sections. The initial few weeks of the project were spent replicating the results and techniques found in [15]. Discussion was had on the subject of which algorithm would be optimal for updating the system over time. Algorithms such as Gillespie[17] and τ-leaping [18] were proposed, but

4 Proposal

- Writing paper on growth dependent stuffs
- begin work on more intricate continuum model - surface roughness and flow
- utilise data from AkzoNobel to accurately model growth

- visit AkzoNobel to undertake lab work and metagenomic analysis

In this section, detail, as far as you are currently able, your research plan for the second and third years of your PhD, drawing from the key references [**?**] that you have highlighted in your review section. Here, try and illustrate your proposal, as in Figure 1 which is taken from the same paper as the illustration references.

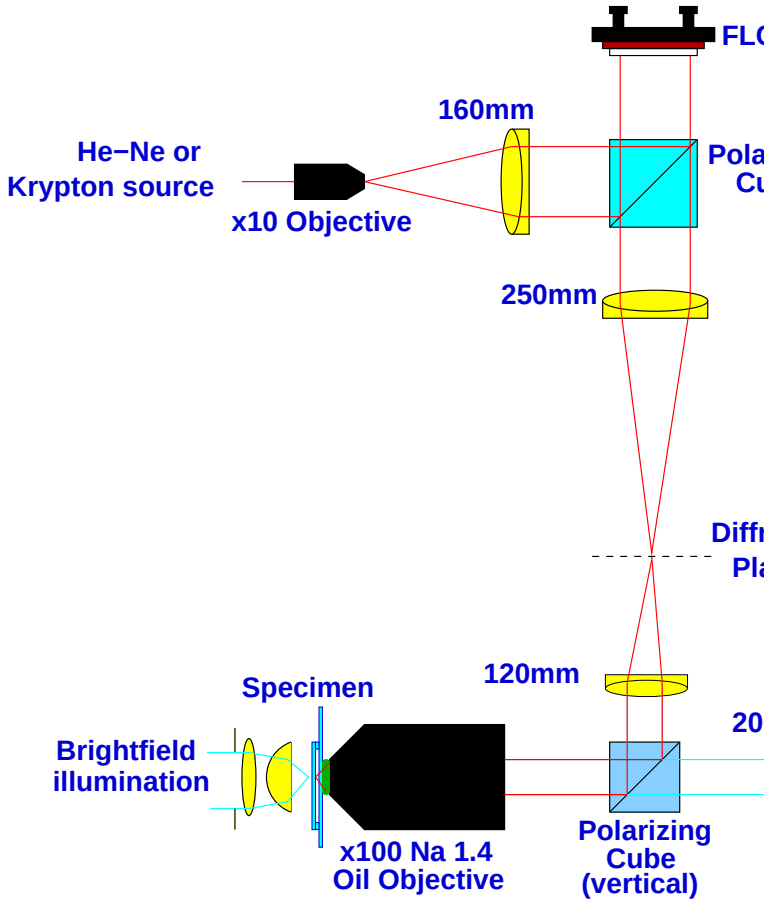

Figure 1: Here is the optical system from the same paper as the reference drawn in `xfig` and include to shown how such a figure in included.

At this stage it is *not* expected that this will be a fully-developed research proposal, but is your chance to show what you have extracted from the literature and how you see your own work will fit in. This section is not expected to exceed 2 pages.

5 Summary

As short section highlighting the key aspect of your proposal. At this stage this may be a bit uncertain and will be subject to charge as the work progresses.

References

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[15] Philip Greulich, Bartłomiej Waclaw, and Rosalind J. Allen. Mutational pathway determines whether drug gradients accelerate evolution of drug-resistant cells. *Phys. Rev. Lett.*, 109:088101, Aug 2012.

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