Objective:

To adapt the Nowak’s evolutionary epidemiology model to how malaria vaccines (RTS,S/AS01 and R21/Matrix-M) are changing the dynamics of Plasmodium.

Problem:

**Pathogen**: *Plasmodium* (mainly *P. falciparum* and *P. vivax*).

**Vector**: Female *Anopheles* mosquito.

**Superinfection**: >100 strains per species → contributes to superinfection and high genetic variability. Infection with multiple genetically distinct *Plasmodium* strains at once - contradicts simplified models that assume strain exclusion.

Content:

1. [Model vaccines impact with Nowak's equations + assumptions](#chapter1) (1-4)

* [11.1 - Basic Epidemiological Dynamics of a Host-Parasite Interaction](#chapter11) (1-2)
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Model Nowak’s equations + assumptions

To model the impact of recent malaria vaccines, we will use the equations presented in Chapter 11 of *Evolutionary Dynamics: Exploring the Equations of Life* by Martin Nowak.

We begin by **assuming** that Nowak's model accurately reflects the real-world dynamics of Plasmodium parasite infections. Based on this framework, we will identify which parameters are likely affected by vaccination, allowing us to compare two scenarios: one **without vaccination** and one **with** the malaria vaccines RTS,S/AS01 (Mosquirix) and R21/Matrix-M.

11.1 - Basic Epidemiological Dynamics of a Host-Parasite Interaction

**The case of no vaccine used:**

The basic dynamics of a host-parasite interaction are described by the following system of differential equations (Equation 11.1, p. 192):

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Where:

x(t) – is the population of the uninfected hosts

y(t) – infected host

k – the newcoming rate (immigration + birth rate)

u – natural death rate

v – virulence – excess morality - extra death rate caused by malaria

β – the infection rate of malaria (from infected to uninfected)

**The case of (Mosquirix) and R21/Matrix-M used:**

Both RTS,S/AS01 (Mosquirix) and R21/Matrix-M target the *sporozoite* stage of the Plasmodium life cycle, which is the phase when the parasite is injected into the human host by a mosquito. These vaccines aim to neutralize the parasite before it can establish an infection in the liver, thus decrease the chance of getting infected β. All of the other terms depend indirectly on the change of e.

Let be the transmission rate when vaccine i is used. And be efficacy of the vaccine i.

The conditions:

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The only linear way of modelling is .

It can be thought as the following. The vaccine i stops % of the parasite that have entered the hosts body (those that are included in the rate. This means that (1-)% out of has still survived. Meaning that the new rate of the new infects is the (1-) of the initial one. Thus .

For **RTS,S/AS01 (Mosquirix):**

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For **R21/Matrix-M**:

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With:

– is the efficacy of **RTS,S/AS01 (Mosquirix)**

– is the efficacy of the **R21/Matrix-M**

It is acknowledged that RTS,S/AS01 (Mosquirix) has a longer history, and the efficacy of the vaccine was calculated on the basis of data collected over a more extended period. Consequently, the efficacy of R21/Matrix-M may in fact be reduced over time.

We will start with modelling malaria with the simplest models to understand how it all works and gradually come to superinfection modelling.

Basic Reproductive Ratio for 11.1

Using relational, we can derive a new model for :

To prevent epidemic is a necessary condition.

From that we can derive the minimum efficacy of the vaccine needed to prevent epidemic:

This might be useful to model by how much vaccines with different efficacy differ.

To see how the theory in Nowak’s book reflects of the malaria disease we can later model x(t) &y(t) to look at the behaviour of the malaria in long term.

And to see what numbers they are going to settle on we can use:

The last 2 formulas are derived from:

As and are the population, of the susceptible and infected by the parasite I respectfully, at the equilibrium that the system settles down to after damping oscillations.

11.2 Selection Maximises

The theory says that that evolution will tent to maximise in the environment where there are multiple stains, which is the case for malaria. This is to outcompete the other strains by effecting langer population then the other strains.

To do that parasite will tent to increase and decrease .

To see if that is the case for malaria we will try to model .

11.3 Superinfection

The formulas provided in this part of chapter 11 assume that the infects are susceptible to another infection and that the infection of a single host is always dominated by one parasite strain.

Let the value of the strain with higher coefficient, be higher than any of the variances with lower coefficient, i.

ODEs for environment with malaria vaccine:

Where:

s – the rate of superinfection.

Using that we can potentially model multiple strains at the same time.

Code + Plots:

Both of the WWO-approved vaccines, *RTS,S/AS01 (Mosquirix) and R21/Matrix-M*, are used in sub-Saharan Africa to combat Plasmodium falciparum. So that is the region that we are going to test our assumptions on. R21/Matrix-M is a more modern vaccine and, as it is not yet widely used, there is less data available for it. We will use Python to test the models.

**Plan for this chapter:**

1. Test the models **with hypothetically reasonable numbers**. This will show how the models behave under the assumed conditions.
2. Test with **real** **data**.

**Modelling Using Hypothetical data:**

| **Parameter** | **Symbol** | **Value** | **Explanation** |
| --- | --- | --- | --- |
| Total population | N | 100,000 | Smaller population for clearer visualization |
| Recruitment rate | k | 1,000 | Birth rate per year |
| Natural death rate | u | 0.02 | Per year |
| Disease-induced death rate | v | 0.3 | High mortality |
| Transmission rate | β | 3.0 | High transmission rate per year |
| Initial susceptible | x(0) | 99,000 | Susceptible at start |
| Initial infected | y(0) | 1,000 | Infected at start |
| Vaccine efficacies | ei | 0.0, 0.33, 0.77 | Same as before |

– no vaccine is used

– **RTS,S/AS01 (Mosquirix)**

– **R21/Matrix-M**

Code for 11.1 (:

We are going to use conclusions from [11.1 - Basic Epidemiological Dynamics of a Host-Parasite Interaction](#chapter11) part:

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Изображение выглядит как текст, линия, График, диаграмма

Содержимое, созданное искусственным интеллектом, может быть неверным.

Name of the code - basic\_dynamics.py

Modelling for [Basic Reproductive Ratio for 11.1](#chapter112) (2-3)

Изображение выглядит как текст, линия, График, диаграмма

Содержимое, созданное искусственным интеллектом, может быть неверным.

Name R0\_analysis1.py

Изображение выглядит как диаграмма, зарисовка, линия, рисунок

Содержимое, созданное искусственным интеллектом, может быть неверным.

Name R0\_analysis2.py

Modelling [11.3 - Superinfection](#chapter13) (3-4)

s=0.5

n=3

Изображение выглядит как линия, График, диаграмма, текст

Содержимое, созданное искусственным интеллектом, может быть неверным.

Name superinfection\_model.py

Modelling using WWO Reports

| **Country / Region** | **Year** | **Vaccine** | **Strain ii** | **yiy\_i (prevalence)** |
| --- | --- | --- | --- | --- |
| Burkina Faso | 2023 | RTS,S/AS01 | 1 | Varies by prevalence (e.g., % clones) |
| Burkina Faso / others | 2023 | R21/Matrix‑M | 1 | Similar distribution |

| **Country / Region** | **eie\_i (vaccine efficacy)** | **vi (recovery rate)** | **s (superinfection factor)** | **kk, uu (birth, death rates)** | **ββ** |
| --- | --- | --- | --- | --- | --- |
| Burkina Faso | ~0.40–0.56 ([WIRED](https://www.wired.com/story/malaria-vaccine-oxford-approval?utm_source=chatgpt.com), [Wikipedia](https://en.wikipedia.org/wiki/RTS%2CS?utm_source=chatgpt.com), [World Health Organization](https://www.who.int/news-room/questions-and-answers/item/q-a-on-rts-s-malaria-vaccine/?utm_source=chatgpt.com)) | ~1/14 ≈ 0.071/day | 2–3 |  |  |
| Burkina Faso / others | ~0.75([The Times](https://www.thetimes.co.uk/article/british-doctor-nearly-killed-by-malaria-helps-develop-new-vaccine-c3jx7lgts?utm_source=chatgpt.com), [Reuters](https://www.reuters.com/business/healthcare-pharmaceuticals/second-malaria-vaccine-launched-ivory-coast-new-milestone-2024-07-15/?utm_source=chatgpt.com), [Wikipedia](https://en.wikipedia.org/wiki/Malaria_vaccine?utm_source=chatgpt.com), [Vaccine Knowledge](https://vaccineknowledge.ox.ac.uk/malaria-vaccine?utm_source=chatgpt.com)) | ~0.071/day | 2-3 |  |  |

Analysis of Results

**Why is linear?**

That was the simplest way to model it; there was no need to overcomplicate things. However, time is the main factor causing changes in e\_i. All the data sets show that vaccine immunity decreases over time, which explains the need for revaccination. Furthermore, it seems that the rate at which decreases is increasing, suggesting that the scale factor of is not linear. Assuming the same natural conditions:

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The possible factor that we can multiply by is .

Suggestion:

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Analyse of the current model:

Изображение выглядит как диаграмма, зарисовка, линия, рисунок

Содержимое, созданное искусственным интеллектом, может быть неверным.

Name R0\_analysis2.py

We can see that is maximised when both v and e are small. It also shows that when having large enough malaria vaccine efficacy, it is highly likely that will be less then 1, for almost any values of v. This suggests that with the vaccine with the high efficacy it is possible to stop highly virulent malaria.