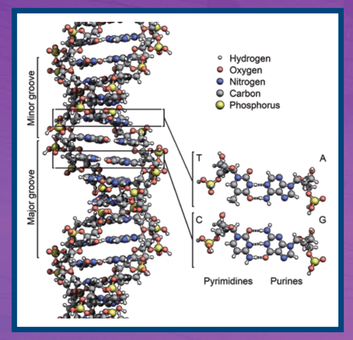
Why do we get cancer?!

Konstantin Gizdov
Institute for Complex Systems & Mathematical Biology, University of Aberdeen

What is the problem?

Our bodies are made of 40 trillion cells. Each of those cells contains a complete and "perfect" copy of an individual's DNA. That means that from the first cell (the zygote) a person's DNA needs to be copied at least 40 trillion times in order to make a full-grown human. How many times do you think you can copy something before making a mistake? How about when you are also trying to survive against a viral or bacterial attack? Add in working with scarcity of food. This is the average life of a cell in our body. Cells need to grow and multiply, but they often do so in less than ideal conditions. Interference in the normal cell cycle can lead to errors in DNA replication, rapid mutations and cell death. Sometimes however, the mutations lead to cancer. So we as scientists must investigate and find out how DNA replicates and how we can prevent it from mutating into cancerous DNA.



Model of DNA

How big a problem is it?

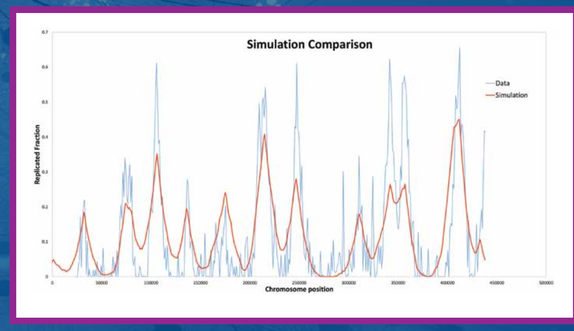
Replicating its genome correctly is the core process of any species' survival and reproduction success. It is thus very important to human health as well. Understanding the details and intricacies of this process is vital for ensuring scientists and doctors can continue to develop effective cures for complex diseases such as cancer.

How did my research help?

Developing a successful model of how DNA is replicated in harsh conditions is essential to developing a deeper understanding of the process. Regardless of the simplistic nature of my analysis, I was able to help my supervisor identify key areas of interest, that were later deeply investigated by him and his colleagues in a scientific paper that would serve other scientists in this field to further their research. (Hawkins, M. *et al.*, High-Resolution Replication Profiles Define the Stochastic Nature of Genome Replication Initiation and Termination. *Cell Reports*, Vol,5, Issue 4, p1132–1141, 27 November 2013)

What did we do?

In the process of studying DNA replication I discovered several exciting things. Firstly, eukaryotic cells would try in any case to replicate their telomeres. This could be because maintaining telomeres' integrity is vital for preventing cancer cell formation. Also, replication forks tend to exhibit an interesting failsafe mechanism of detaching themselves from DNA if it is likely they will cause DNA damage.



How did I do it?

The main tools I used in this project were mathematics and programming. In order to understand the behaviour of the replication machinery in this type of situation, I needed first to formulate a mathematical model of a single idealised replication fork. Then, using computer programming, I developed simulations where I combined several replication forks in a similar way to how a cell would combine them to replicate its own DNA. Then by adjusting the conditions in those simulations, I was able to investigate how DNA replication is affected by different parameters including things like dNTP abundance, timing and failure rate.

$$\frac{\partial[dNTP]}{\partial t} = -2N_{forks}V_{forks}$$

$$V_{fork} = \frac{\partial x}{\partial t}_{fork} = \frac{[dNTP]}{\tau_0}$$

Where is the link to human health?

Understanding DNA replication in harsh conditions is very important. It can give insights on what are the underlying causes for DNA damage and what type of processes may contribute to cancer nucleation.

Who am I?

I am now a 4th year Physics student in the University of Aberdeen. Over the last summer I took part in the University's iGEM team, developing a rapid diagnostic method for Sleeping Sickness, with the hope of saving millions of people. We will be presenting our project in front of 3,000 other students at the iGEM Jamboree this November at MIT, Boston. I am also now starting work on my Honours project (Dissertation) about the theory of Quantum Gravity.

During the course of my university degree I have gained experience and developed vital skills for my future. With the help of organisations such as Medical Research Scotland, I have also had the opportunity to apply those to real-world problems. This has given me the edge to pursue an exciting career in science.

Konstantin was supervised during his Vacation Research Scholarship, *"Mathematical modelling of DNA replication in conditions of dNTP scarcity"* by Dr Alessandro Moura.