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Modelling the Mutation Rate of The Flash in Context

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Abstract
The Flash has had many incarnations, however all share key characteristics. One of these is an increased metabolic rate and therefore an increased cell turnover. A simple model is used to model the cell turnover of the Flash and calculate the rate at which he acquires mutations, 1.71×10^{15} mutations per day. This is compared to the incidence of cancer in the UK, showing the Flash has an increased risk.

Introduction
The Flash is the fastest man alive. He is also one of DC comics' most iconic characters and has been portrayed by different individuals [1]. However, all iterations share a similar repertoire of speed-orientated abilities. One such power is undergoing of accelerated metabolism, and therefore cell turnover.

As part of the normal cell cycle, the genome is completely copied through a semi-conservative replication process. This process utilises a replication fork, with a leading and lagging strand. The leading strand utilises a DNA Polymerase to synthesise the new DNA strand in a 5' to 3' direction. Replication at the lagging strand is more complex as it requires Okasaki's fragments joined by DNA ligase enzymes [2].

The replication process is not perfect and as such mutations can occur. Therefore with each replication of the genome, there is a small risk of mutation that has potential to cause pathology within the host [2].

Mistakes within the replication process are combated with DNA repair mechanisms and cell cycle checkpoints [3].

The Knudson Hypothesis
One type of pathology that is caused by mutation is cancer, characterised by uncontrolled cell growth. The pathology caused by cancer can be a result of malignancy, invasive tumours or by the space-occupying effect [4].

On a genetic level, the cause of cancer has been defined by the Knudson, or multiple-hit, hypothesis; which states carcinogenesis is a result of the accumulation of mutations within a cell's DNA. Since the work of Knudson, it is now known the genes involved in this process are oncogenes and tumour suppressor genes [4].

Modelling the Flash's Cell Turnover
It is known the Flash has a higher metabolic rate, evidenced by his increased regenerative capacity. In order to do this the cell division process must occur at a higher rate than that of a normal human, on average once every 24 hours [5].

This rate is not applicable to all human cell types, as each will have their own specialised properties. However for the purpose of this model, it is assumed that all cell types behave in the same way and divide at the maximum rate possible.

In order to maintain the same cell number and therefore cell density, it is assumed the rate apoptosis is equal to the rate of cell proliferation.

Bacterial cells can undergo cell division at a much higher rate, undergoing the process of binary fission. This is mainly due to lack of membrane bound organelles and less complex structure of DNA present within them. The maximum rate of binary fission is one division every 20 minutes, 72 times faster than that of a human [6].

Due to the higher proliferation rate achieved in bacteria, the Flash can be modelled as an organism made up of bacterial cells (a human-sized bacterial colony). The mutation rate in bacterial cells however is greater than eukaryotic cells, mainly due to fewer checkpoint mechanisms. Although modelling the Flash as bacterial cells, the mutation rate will be assumed to be the same as a normal human.

Modelling the Flash's Mutation Rate

The mutation rate for a normal human is 10^{-8} mutations per base pair per division ($bp^{-1}div^{-1}$) [7]. DNA repair mechanisms and cell cycle checkpoints (apoptosis) are able to rectify 99% of all mutations that occur [7]. The resulting mutation rate after repair mechanisms would be 10^{-10} $bp^{-1}div^{-1}$.

This rate can then be applied to the size of the human genome to determine the number of mutations that occur per cell division. The haploid (*n*) genome consists of $3.2x10^9$ base pairs [7]. Human cells are diploid (2*n*), therefore the total number of base pairs contained within each cell can be calculated to be $6.4x10^9$ base pairs. Applying the mutation rate to the diploid genome gives 0.64 mutations per cell division.

Using the assumptions of this model and an estimate for the number of cells in the body to be $3.72x10^{13}$ [8], the total number of mutations acquired after all cells have replicated is $2.38x10^{13}$.

With the rates of cell proliferation previously defined the number of mutations obtained per day for a normal human and the Flash would be $2.38x10^{13}$ and $1.71x10^{15}$ respectively. Using this model the Flash obtains mutations 72 times faster than a normal human, assuming the rate of mutation has a linear correlation with rate of cell proliferation.

In Context

This model can be extrapolated to provide the number of mutations obtained by the Flash over any period of time and compared with the normal human model.

Not all mutations are harmful. Due to redundancy mutations can often be synonymous, leading to no overall change in the proteins produced [2].

However as previously stated, carcinogenesis is a process caused by the accumulation of mutations over time in proto-oncogenes and tumour suppressor genes. This hypothesis is supported by the increase in incidence of cancer amongst the elderly, as over their lifetime they would have accumulated a large number of mutations (see figure 1).

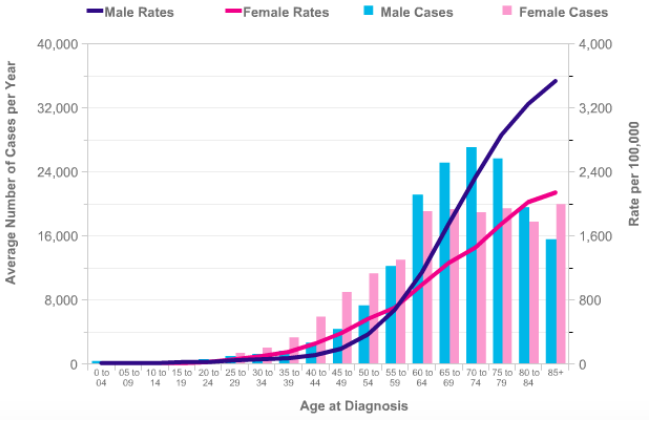

Figure 1 – Incidence Statistics for Cancers (excluding non-melanoma skin cancer) in the UK 2009-11. There is an exponential increase of incidence with age supporting the Knudson Hypothesis [9].

Extrapolating using the model it is found that if the Flash had his speed-related abilities for 1 year, it would be the equivalent of obtaining 72 years worth of mutations, compared to the average human, causing an increased risk of developing cancer.

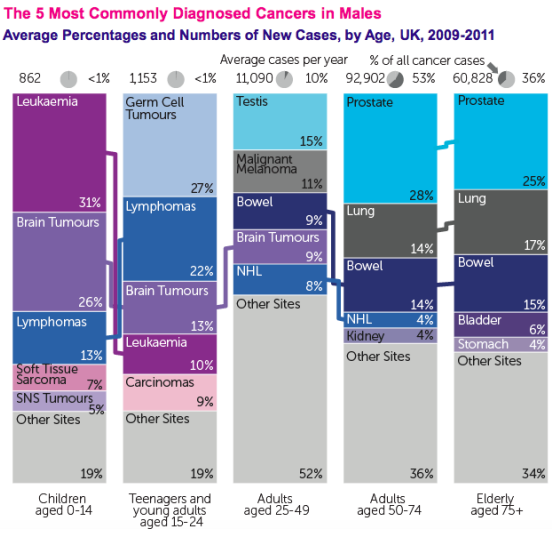

Figure 2 – Most Commonly Age Specific Diagnosed Cancers in Males in the UK (2009-11) [9].

Conclusion

Modelling the Flash as an organism made of bacterial cells allowed the rate of cell turnover and mutations to be calculated to be ~72 times that of an average human. The consequence of this is an increase in the risk of cancer in someone his age, ~25 years old, with a shift in the type of cancer he may develop (see figure 2) towards those usually associated with older age groups.

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