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Adult Neurogenesis in the retina originated in Müller Cells after loss of neurons

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Footnotes

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Abstract

Purpose : Teleost fish have the special property of completely restoring their retina after an injury. More precisely, so-called Müller cells can reprogram their function and contribute to the reproduction of neurons similar to stem cells. It is not known how and how many neurons are produced. We develop a model that describes the development of the cell population following a loss of neurons in the retina. Our goal is to use current biological data to calibrate our model to be able to represent adult neurogenesis and a possible differentiation behavior.

Methods : Our model differs between Müller, progenitor and neuronal cells and we transfer the biological behavior of each cell type in a parameter dependent model resulting in a system of three ordinary differential equations. We take in account

asymmetrical division, symmetrical differentiation and self-renewal. These processes are combined through parameters which are estimated with an in-house software. The fits were performed to a set of published measurements.

Results : We were able to show that the true parameter values are obtained by our fits with a 95% probability. This shows that our model depicts the regenerative process effectively. Analysis of the research data revealed that 5 cell divisions of progenitor cells are needed to make 279 neurons out of 9 Müller cells if we assume that 66% of the Müller cells re-entered the cell cycle after 36 hours.

Conclusions : With our model we were able to show a possible differentiation behavior of the progenitor cells which is still open and we gain a better understanding of the development of the cell populations involved in this process. This could lead to new regenerative treatments for the retina.

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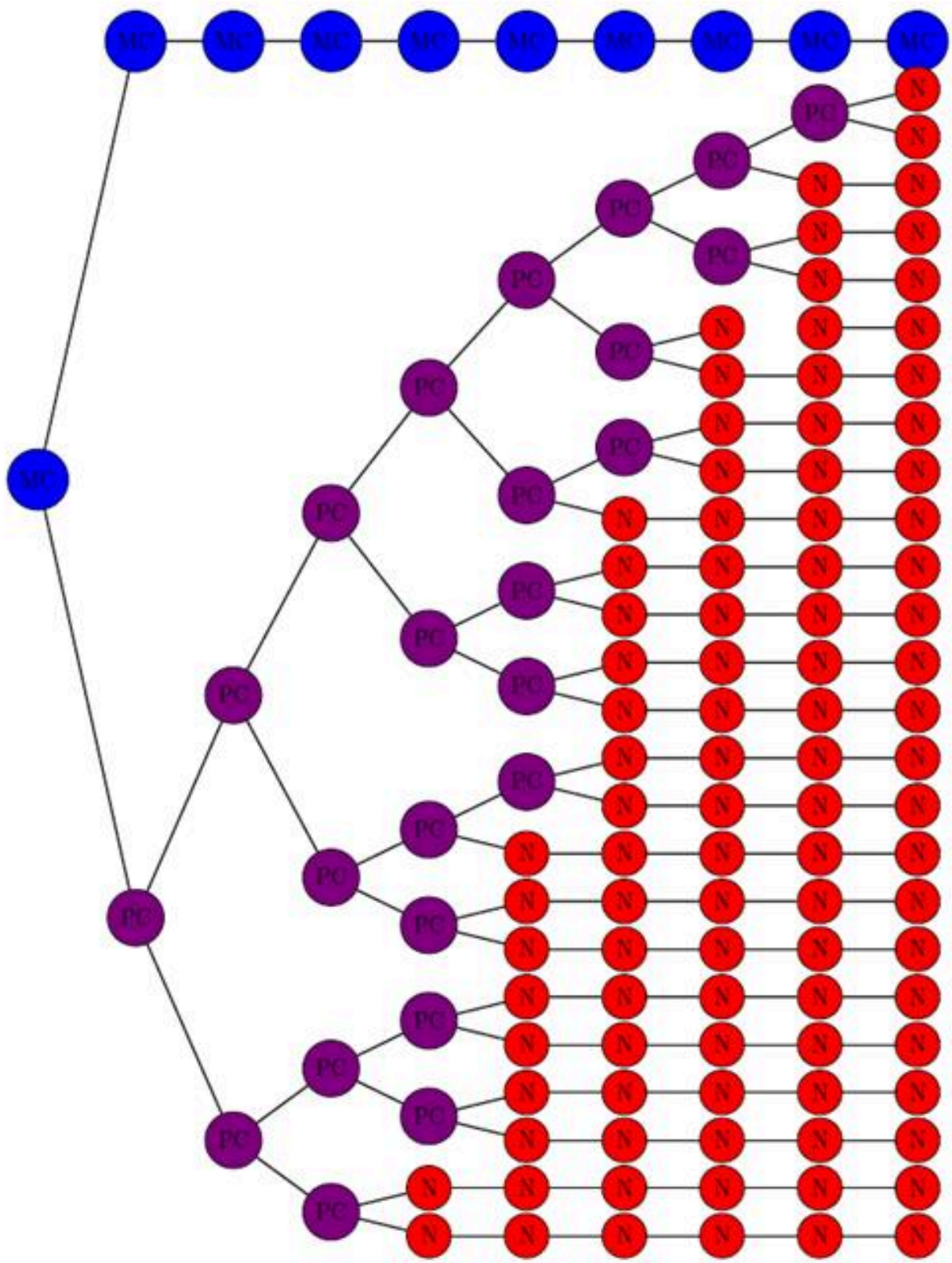

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This Figure presents an exemplary illustration of possible cell developments in adult zebra fish resulting from our mathematical model. We restrict this illustration to the case of one Müller cell (blue) which undergoes an asymmetric cell self-renewal division and divides only once. The number of progenitor cells (purple) can only grow through self-renewal by a combination of asymmetrical division, symmetric differentiation and symmetric self-renewal followed by symmetric differentiation to neurons (red). After 9 cell cycles all neurons are formed.