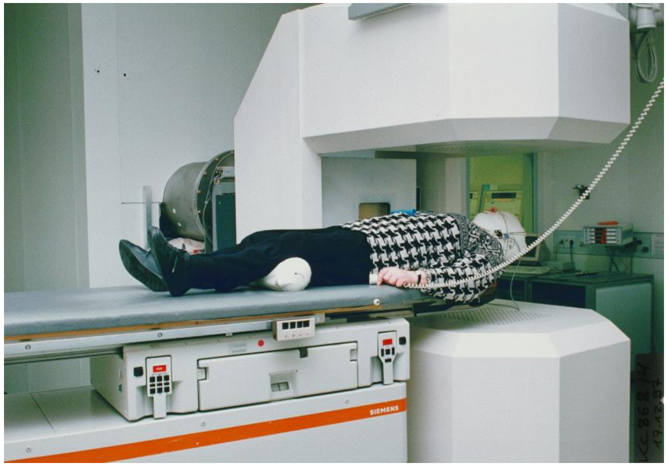
MODELING THE INFLUENCE OF HEAVY ION BEAMS ON THE NEUROGENESIS AND THE FUNCTIONING OF HIPPOCAMPAL NEURAL NETWORKS

E.A. Kolesnikova, A.N. Bugay

Joint Institute for Nuclear Research, Dubna, Russia

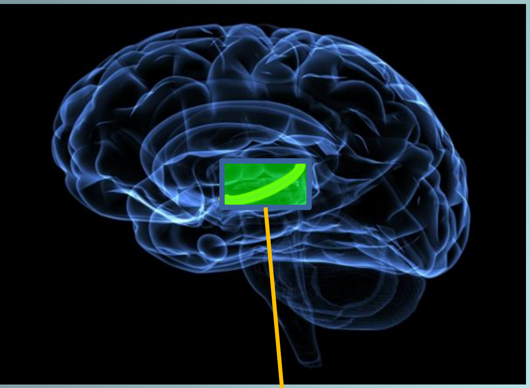
Radiation and CNS

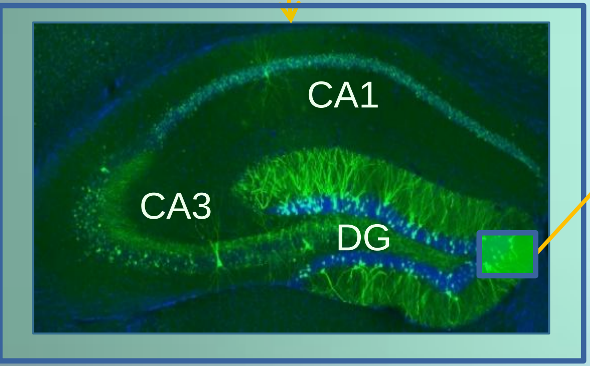


Detriments in cognition and memory are likely to occur after radiation therapy for brain cancer and are also a concern for astronauts exposed to cosmic rays during long-duration space travel.

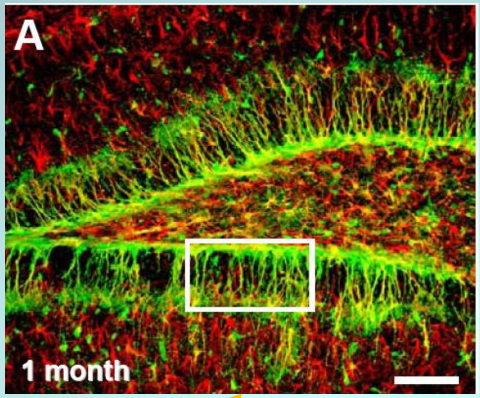
A number of neurocognitive detriments have been reported in clinical studies and animal experiments, including progressive deficits in short- and long-term memory loss, spatial relations, visual motor processing, quantitative skills and impaired learning.

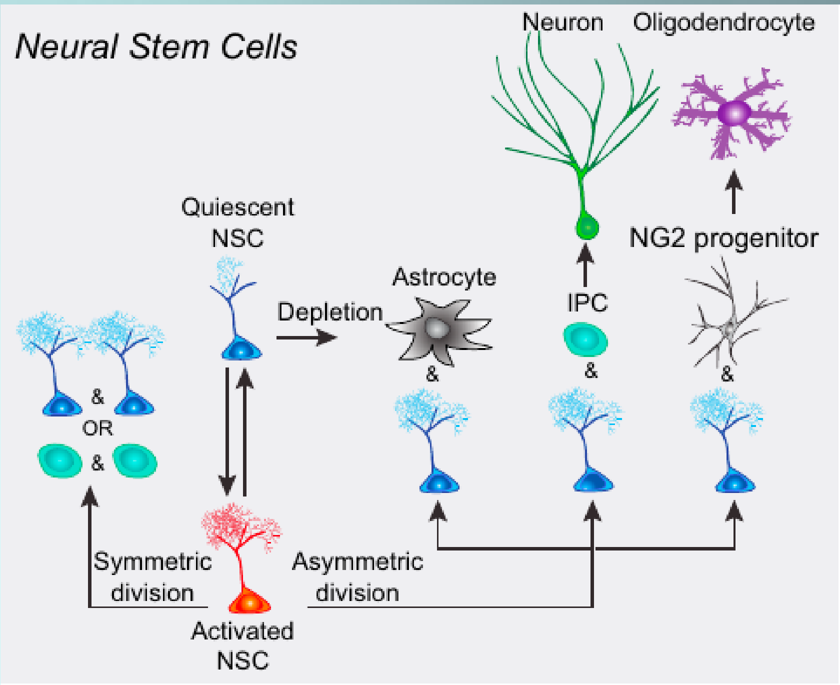
Hippocampal neurogenesis





J. Encinas et al., 2011

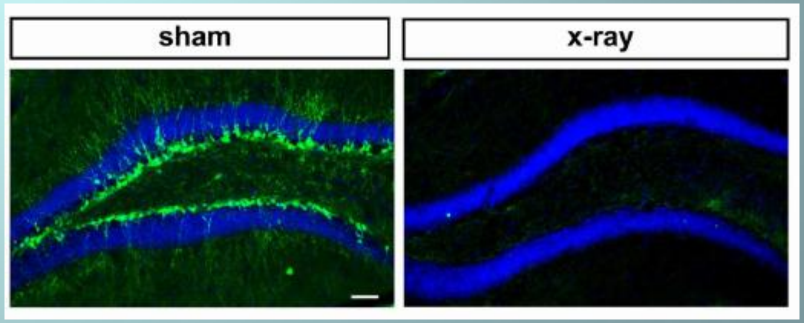




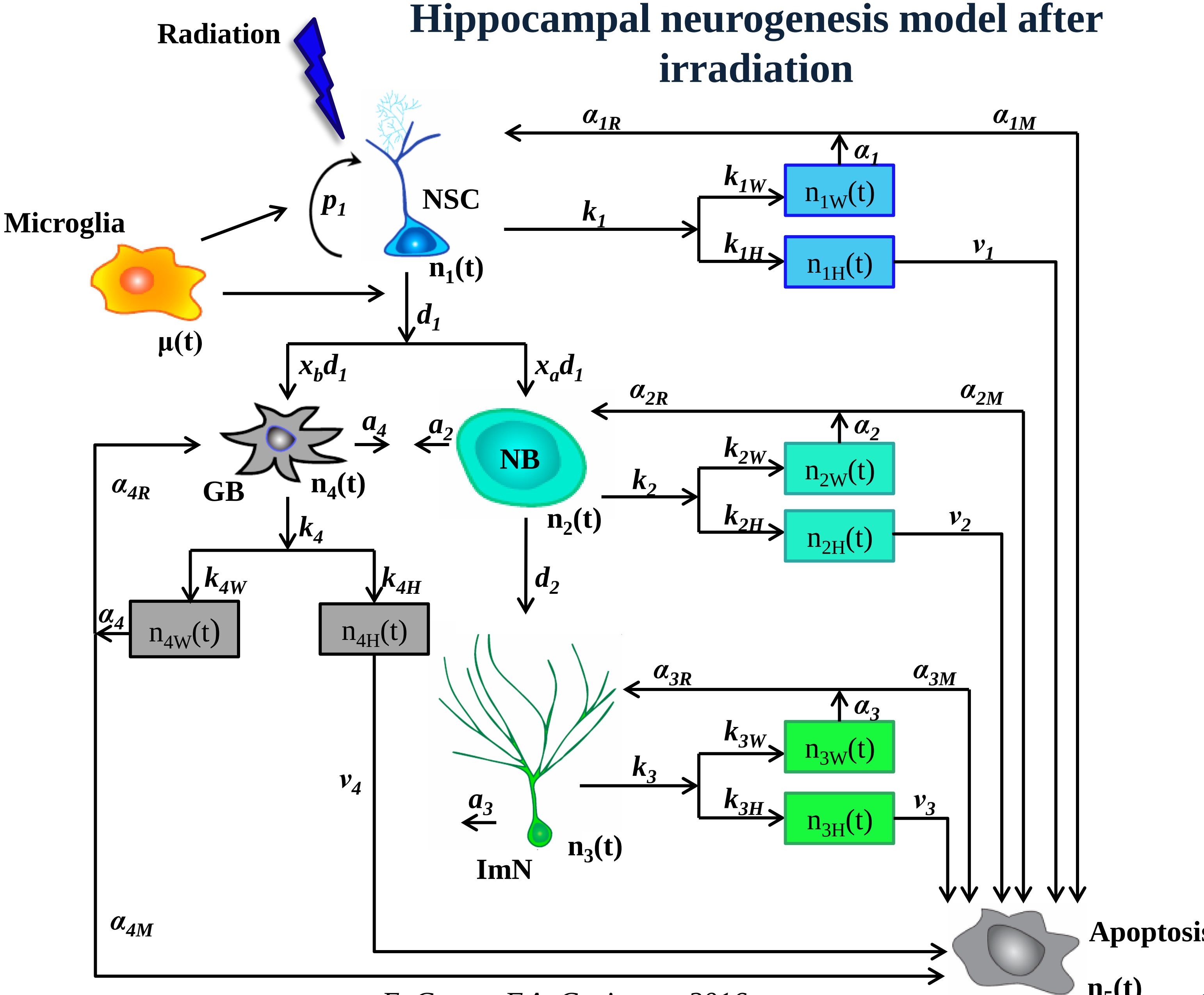
<u>Hippocampus</u>
plays key role in «short-term» and «long-term» memory, integrating processes and plasticity of the brain

<u>Neuronal Stem Cells</u>:

- are localized in the special zones of hippocampus and constantly produce new neurons
- **highly radiosensitive**



Hippocampal neurogenesis model after irradiation



E. Cacao, F.A. Cucinotta, 2016

Mathematical model

Dynamics of neuronal cell population after irradiation can be represented by ordinary differential equations:

$$\frac{dn_1(t)}{dt} = p_1 n_1(t) - d_1 n_1(t) - k_1 n_1(t) + \alpha_{1R} n_{1W}(t)$$

$$\frac{dn_2(t)}{dt} = 2x_a d_1 n_1(t) - d_2 n_2(t) - a_2 n_2(t) - k_2 n_2(t) + \alpha_{2R} n_{2W}(t)$$

$$\frac{dn_3(t)}{dt} = d_2 n_2(t) - a_3 n_3(t) - k_3 n_3(t) + \alpha_{3R} n_{3W}(t)$$

$$\frac{dn_4(t)}{dt} = x_b d_1 n_1(t) - a_4 n_4(t) - k_4 n_4(t) + \alpha_{4R} n_{4W}(t)$$

$$\frac{dn_5(t)}{dt} = \alpha_{2M} n_{2W}(t) + \nu_2 n_{2H}(t) + \alpha_{3M} n_{3W}(t) + \nu_3 n_{3H}(t) - \nu_5 n_5(t)$$

$$\frac{dn_{jW}(t)}{dt} = k_{jW} n_j(t) - \alpha_j n_{jW}(t)$$

$$\frac{dn_{jH}(t)}{dt} = k_{jH} n_j(t) - \nu_j n_{jH}(t), \text{ where } j = 1-4$$

NSC proliferation:

$$\mathrm{p}_1 = \frac{\Psi}{1 + \theta_1 n_1(t) + \theta_2 (n_2(t) + \Phi n_{2W}(t) + \Gamma n_{2H}(t)) + \theta_3 (n_3(t) + \Phi n_{3W}(t) + \Gamma n_{3H}(t)) + \theta_{mg} \mu}$$

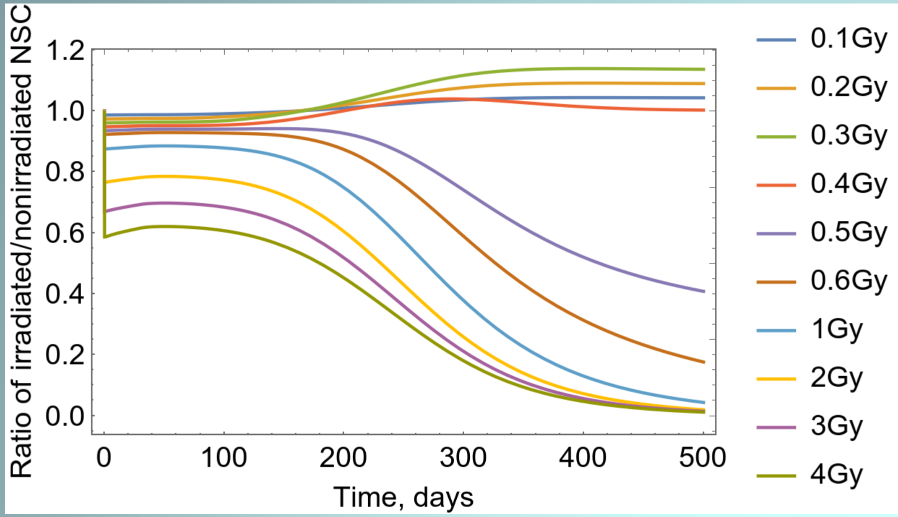
Microglia μ and neurogenic fate Δ

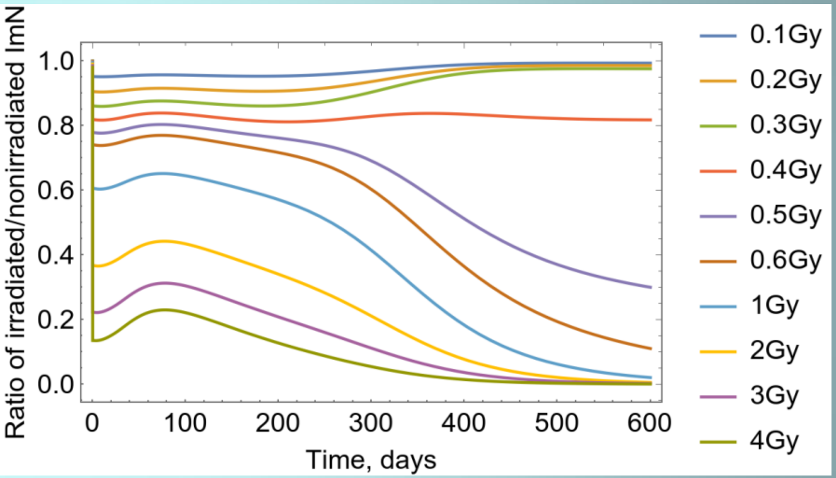
$$\frac{d\mu(\tau)}{dt} = \begin{cases} 0 & \text{for } t < t_d \\ \left[A_0 \dfrac{D}{D + A_1} + B\tau + C\tau^2 \right] e^{-\lambda\tau} & \text{for } t \geq t_d \end{cases}$$

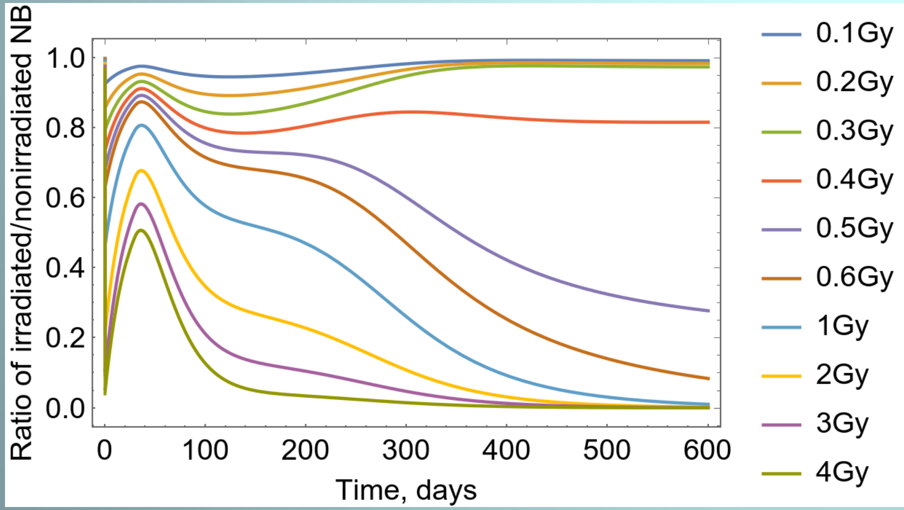
$$\frac{d\Delta(\tau)}{dt} = \begin{cases} 1 & \text{for } t < t_d \\ \left[A_0 \dfrac{D}{D + A_1} + B_0 \mu + B_1 \mu\tau + C\tau^2 \right] e^{-\lambda\tau} & \text{for } t \geq t_d \end{cases}$$

where $\tau = t - t_d$, $t_d = 30$ days

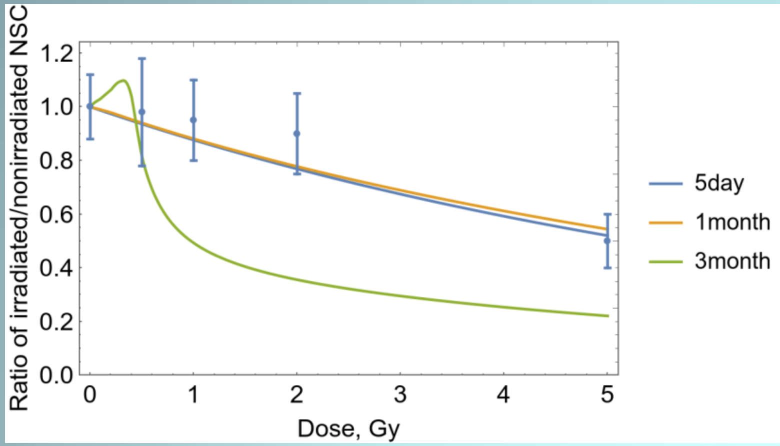
Modeling dynamics of hippocampal neurogenesis after acute exposure to different doses iron radiation

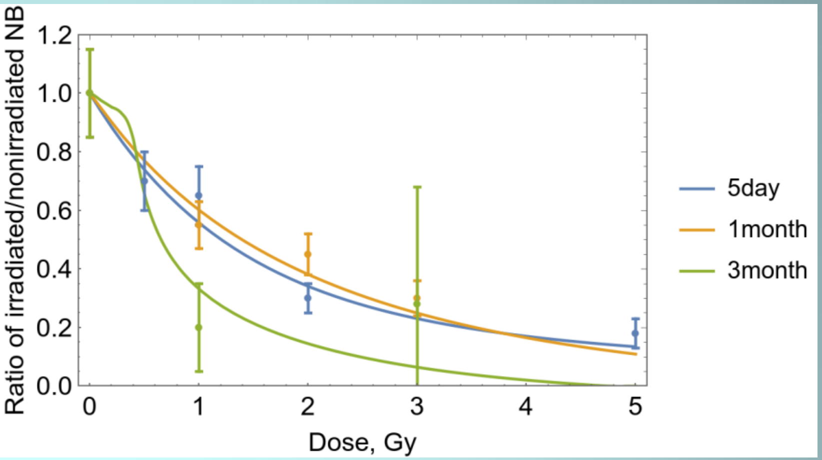


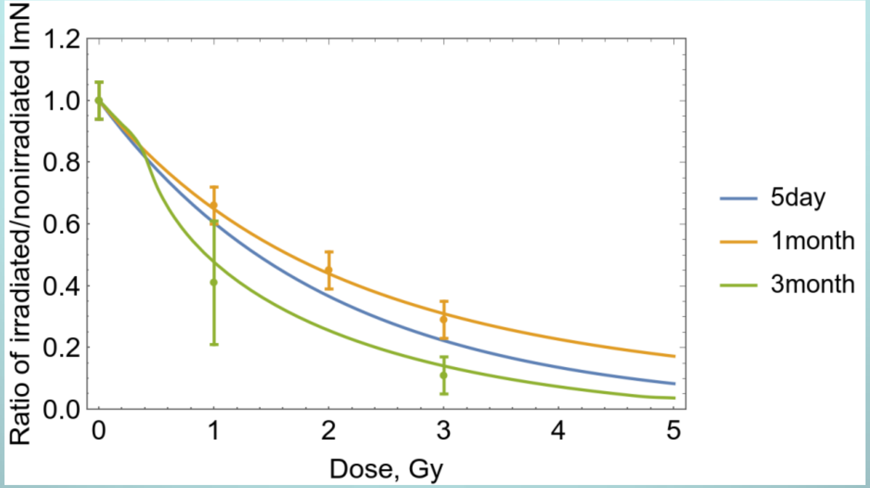




Dose-dependent response of hippocampal neurogenesis to acute exposure of iron radiation

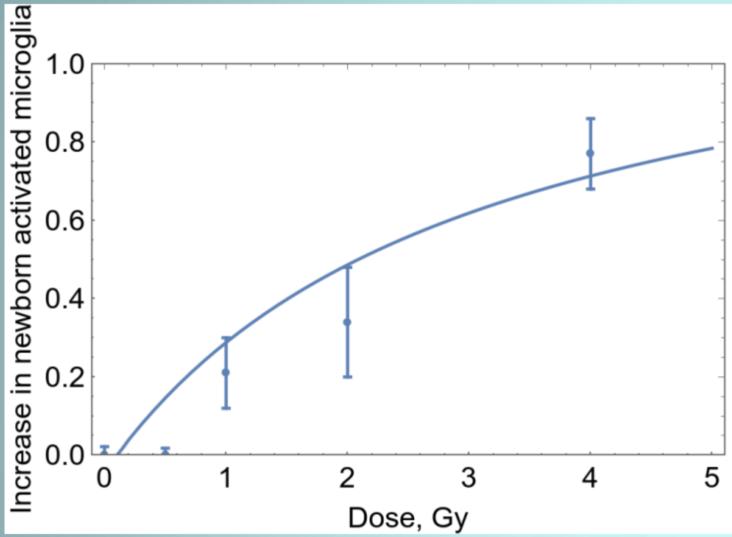


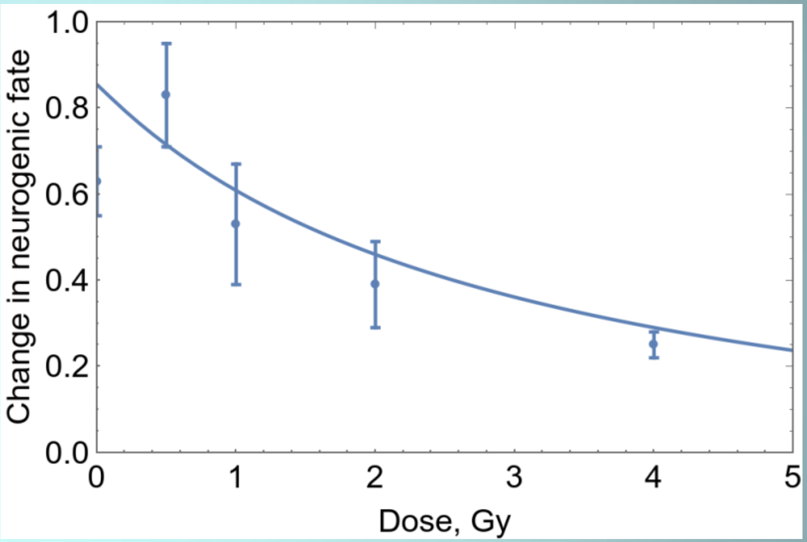




Experimental results – R. Rola et al. 2004, 2005

Newly born activated microglia and change in neurogenic fate at 60 days postirradiation

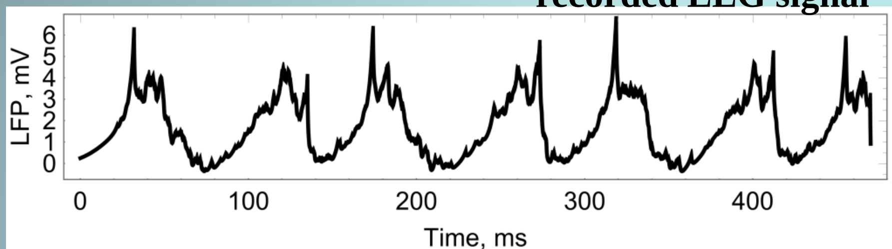


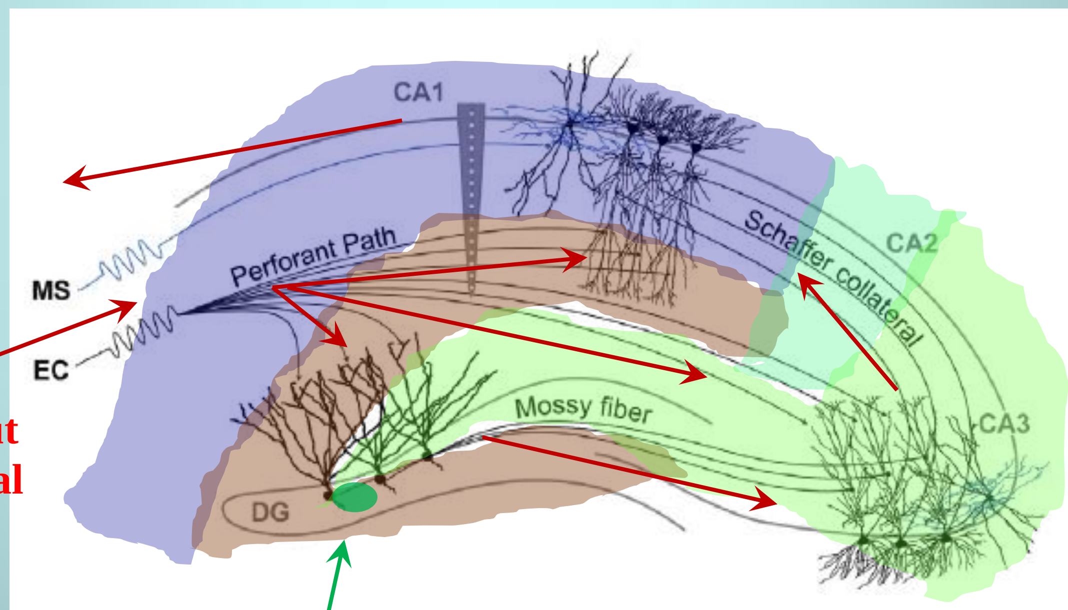


Experimental results – R. Rola et al. 2008

Hippocampal neural networks

recorded EEG signal



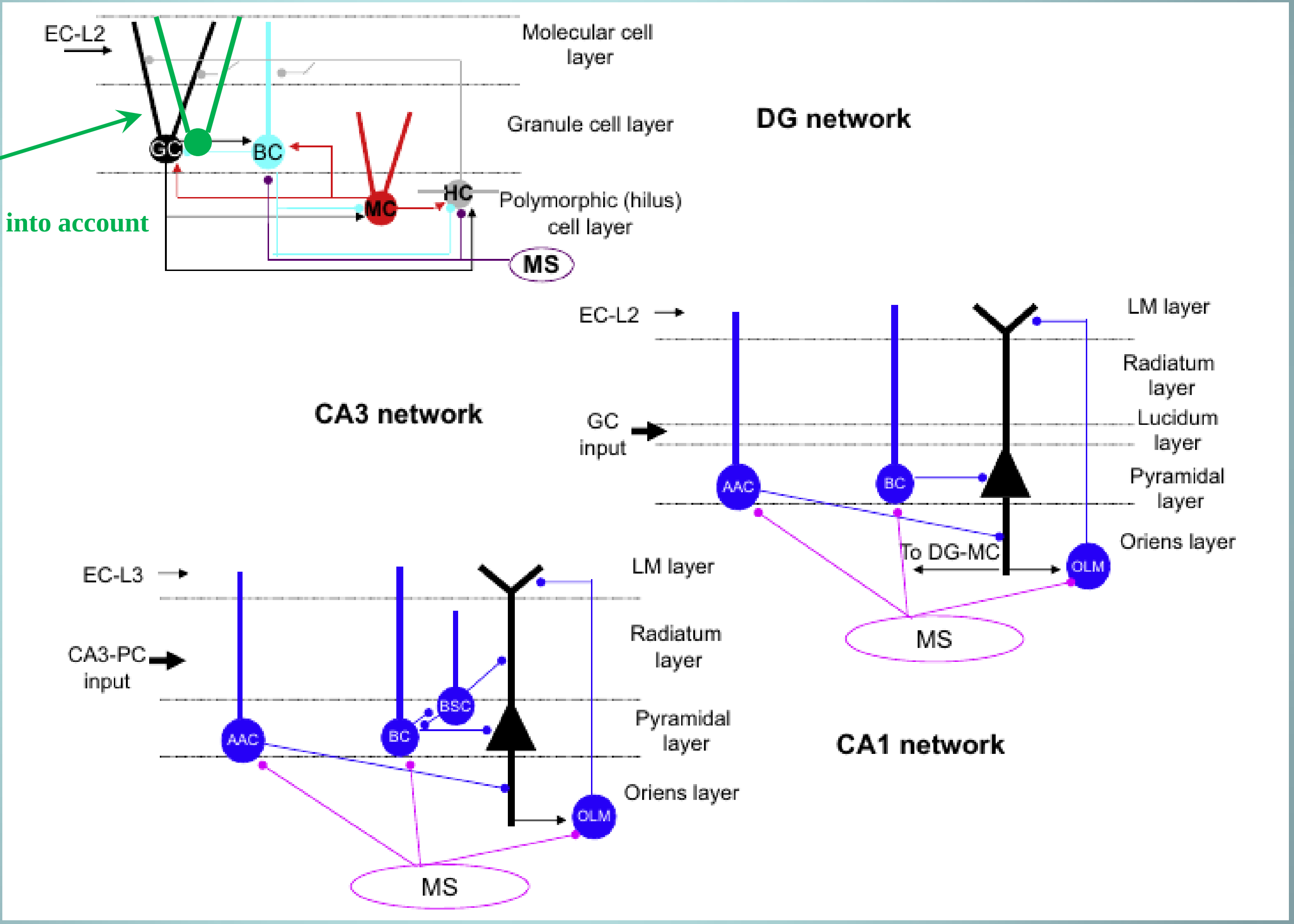


Input signal

Zone of neurogenesis

Neural network architecture

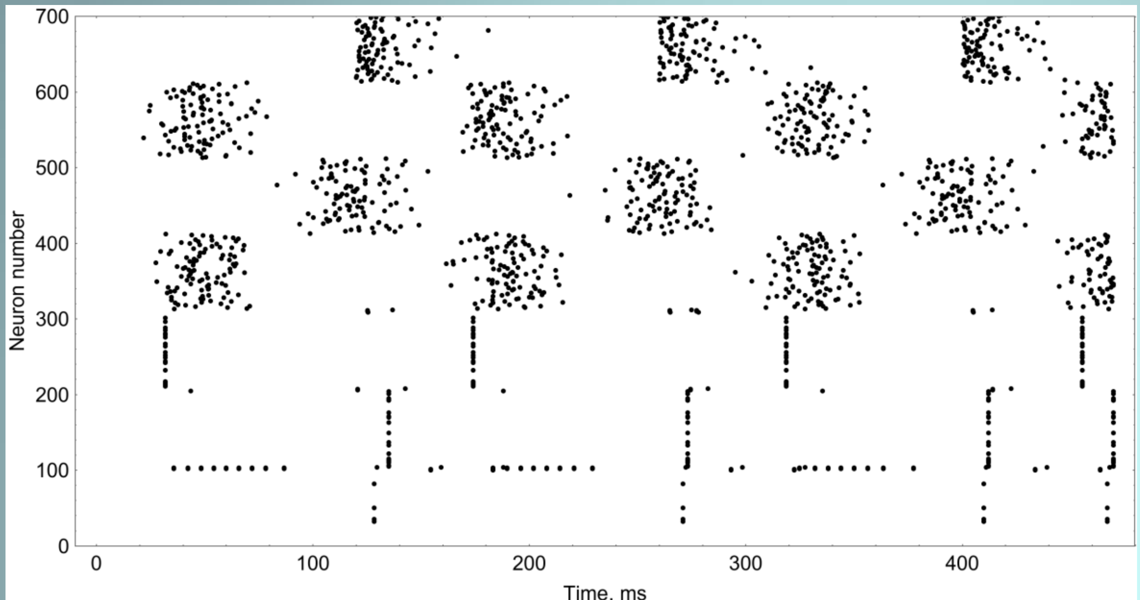
new-born GC are taken into account



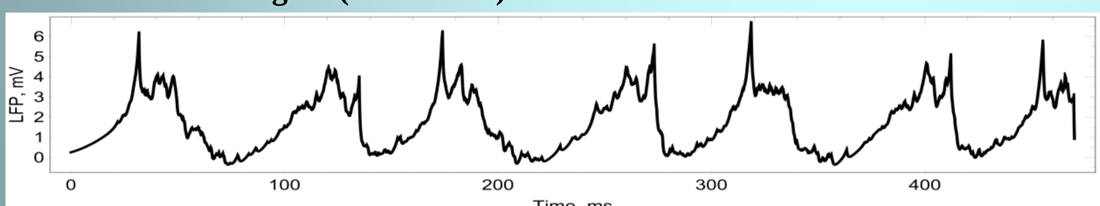
Modified from *V. Cutsuridis, P. Poirazi* (2015)

Neural network activity

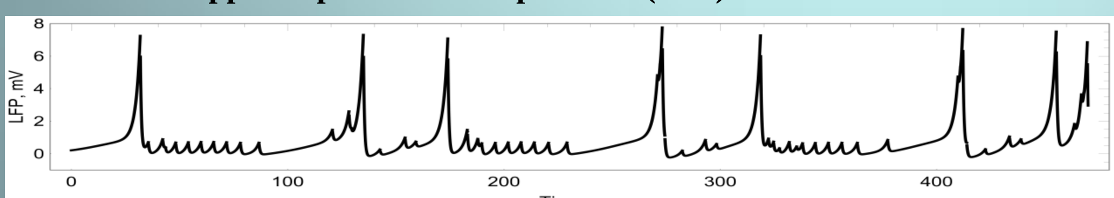
Spike positions



EEG signal (theta wave)

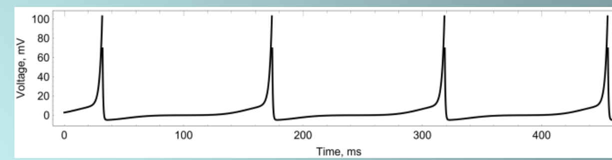


Hippocampal local field potential (LFP)

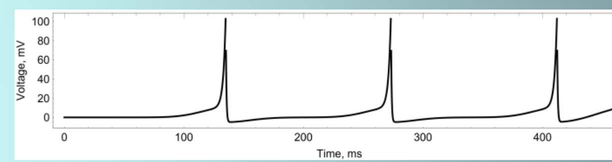


Single cell voltage traces

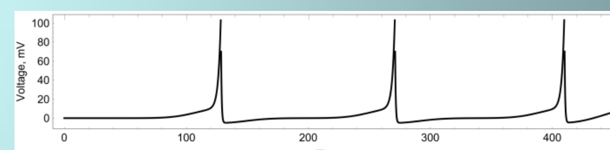
CA1 pyramidal cell



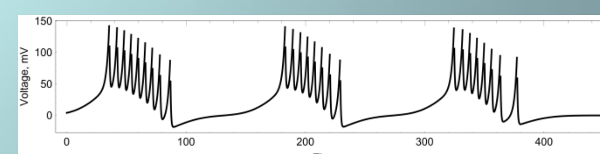
CA3 pyramidal cell



DG granule cell



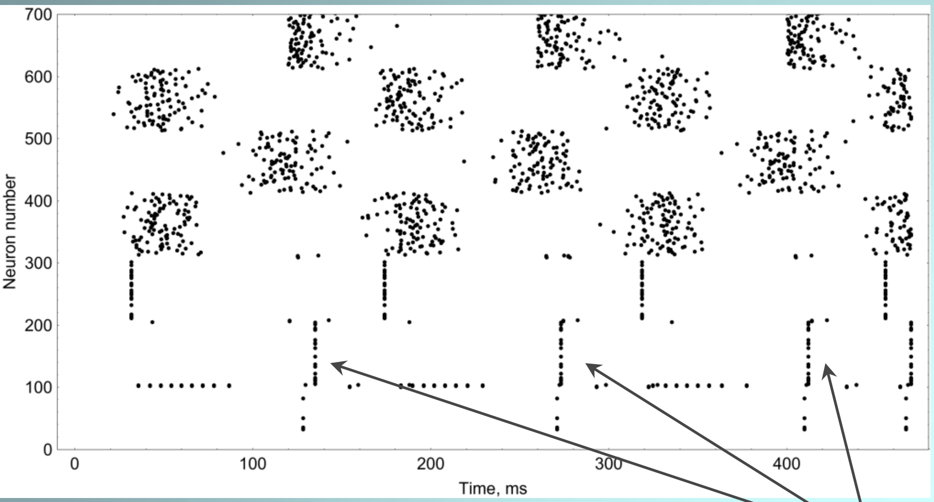
DG basket cell

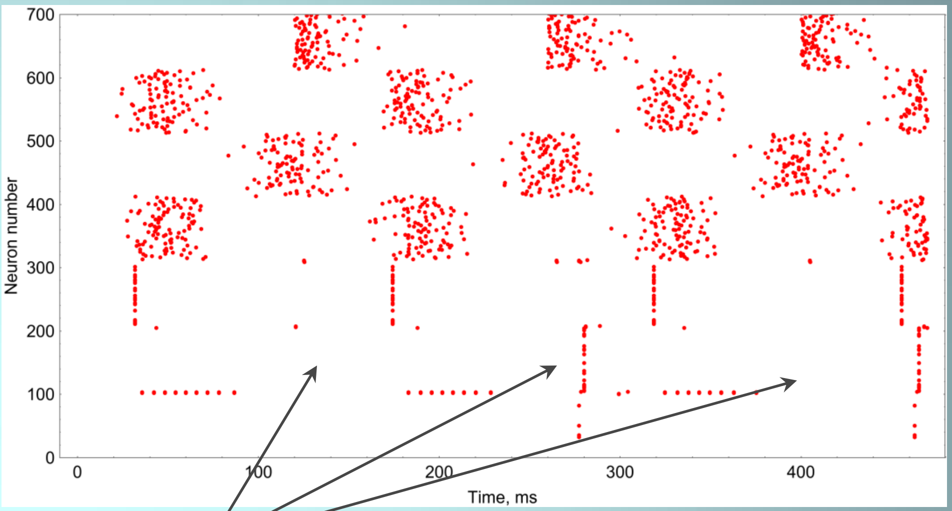


Neural network activity after irradiation

Control

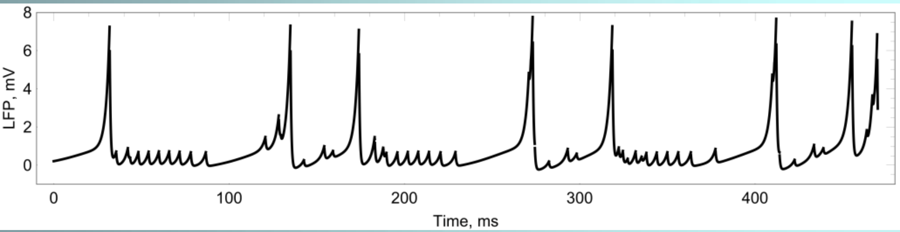
0.8 Gy 600 MeV/u ^{56}Fe

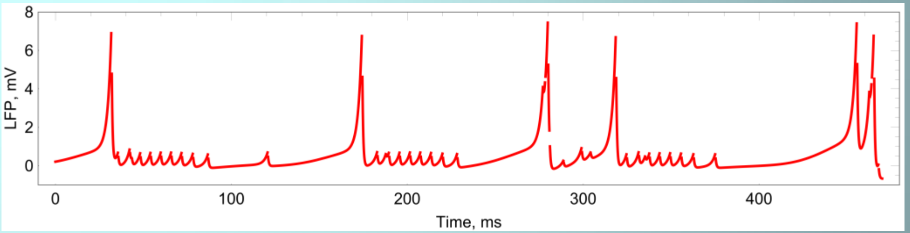


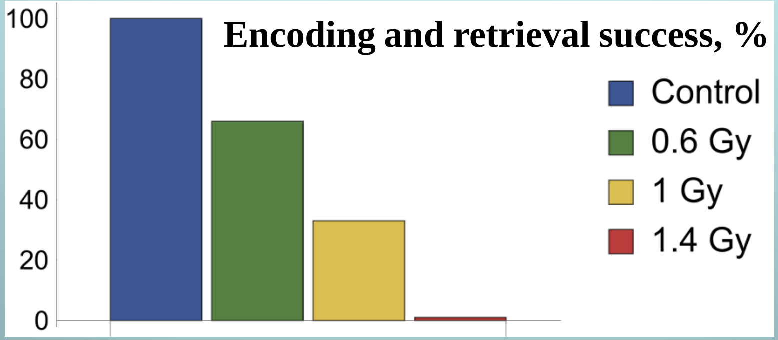


Encoded patterns

hippocampal local field potential







Conclusions

- The effect of radiation on neurogenesis and the work of neural networks was studied.
- It is shown that heavy ions cause non-reversible suppression of neurogenesis.
- Radiation-induced suppression of neurogenesis worsens the processing of information by neural networks.

Thank you for your attention!