Steps towards a virtual lymph node

Sonja Scharf[1,2], Patrick Wurzel[1,2], Jörg Ackermann[1], Martin-Leo Hansmann[2], and Ina Koch[1]

[1] Molecular Bioinformatics, Institute of Computer Science, Goethe-University, Frankfurt am Main
[2] Frankfurt Institute for Advanced Studies, Frankfurt am Main

GOETHE UNIVERSITÄT FRANKFURT AM MAIN

Background: In the lymph node, there are different kinds of cells, for example, B-cells and T-cells. The interaction of the cell types are not fully understood. To investigate cell-cell interactions, we combine 2D slice scans, 3D images and movies of moving cells. The data are from reactive lymph nodes and from lymphomas.

Methods: On 2D slices we have generated cell graphs [1].Using appropriate staining enables us to classify tissue regions in the lymph node. In 3D, we have analyzed the volume of immunohistologically stained cells [2]. The focus of the 4D data is the movement behavior of cells and the characterization of contacts of cells [3]. The data set consists of more than 1000 2D scans, 5000 3D images and 500 movies of lymphatic tissue (adenoids, lymphadenitis, high and low grade lymphomas). Based on this huge data set, generation of the virtual lymph node is possible. Our theoretical starting point to build a systems biological and quantitative model is a Petri Net (PN) [4] of the lymph node [5]. Petri nets are bipartite directed graphs. There are two groups of nodes: active transitions and passive places.

Data set

2D
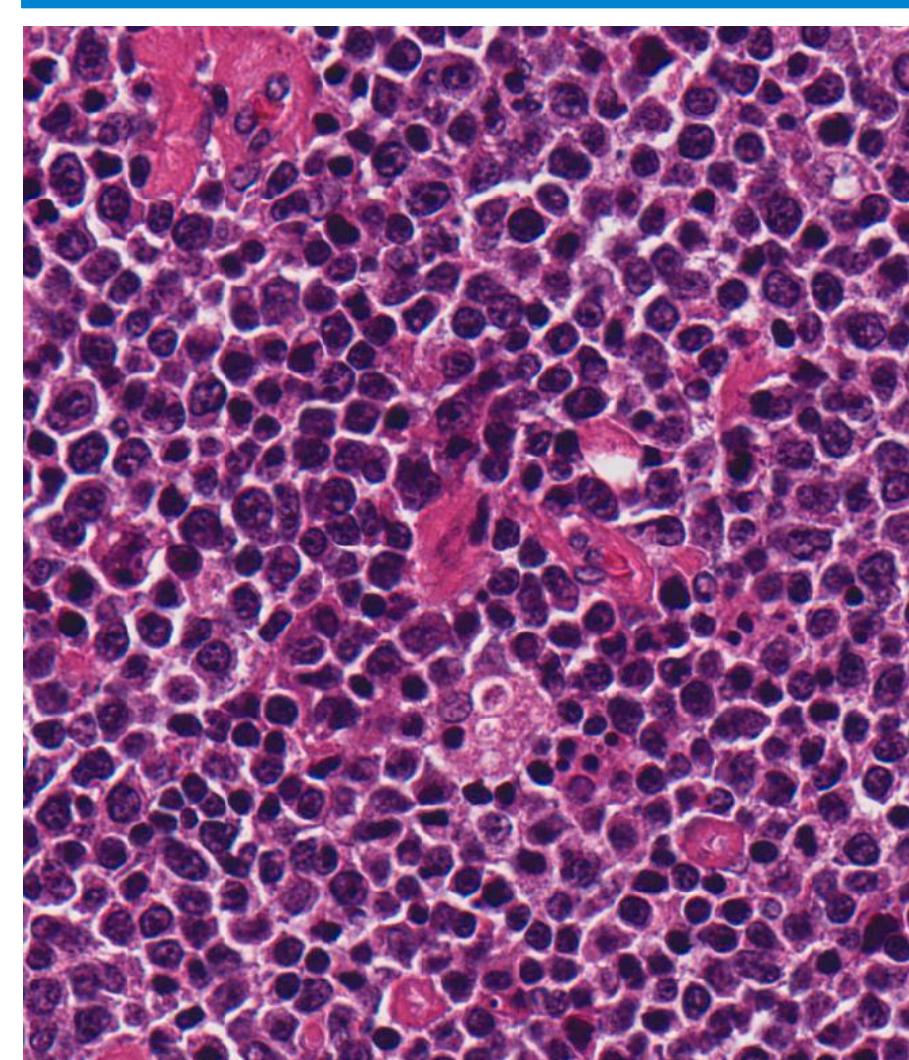
H&E (haematoxylin and eosin stain) images of Diffuse large B-cell lymphoma.
Nuclei are stained in purple and other cell components are stained in red.

3D
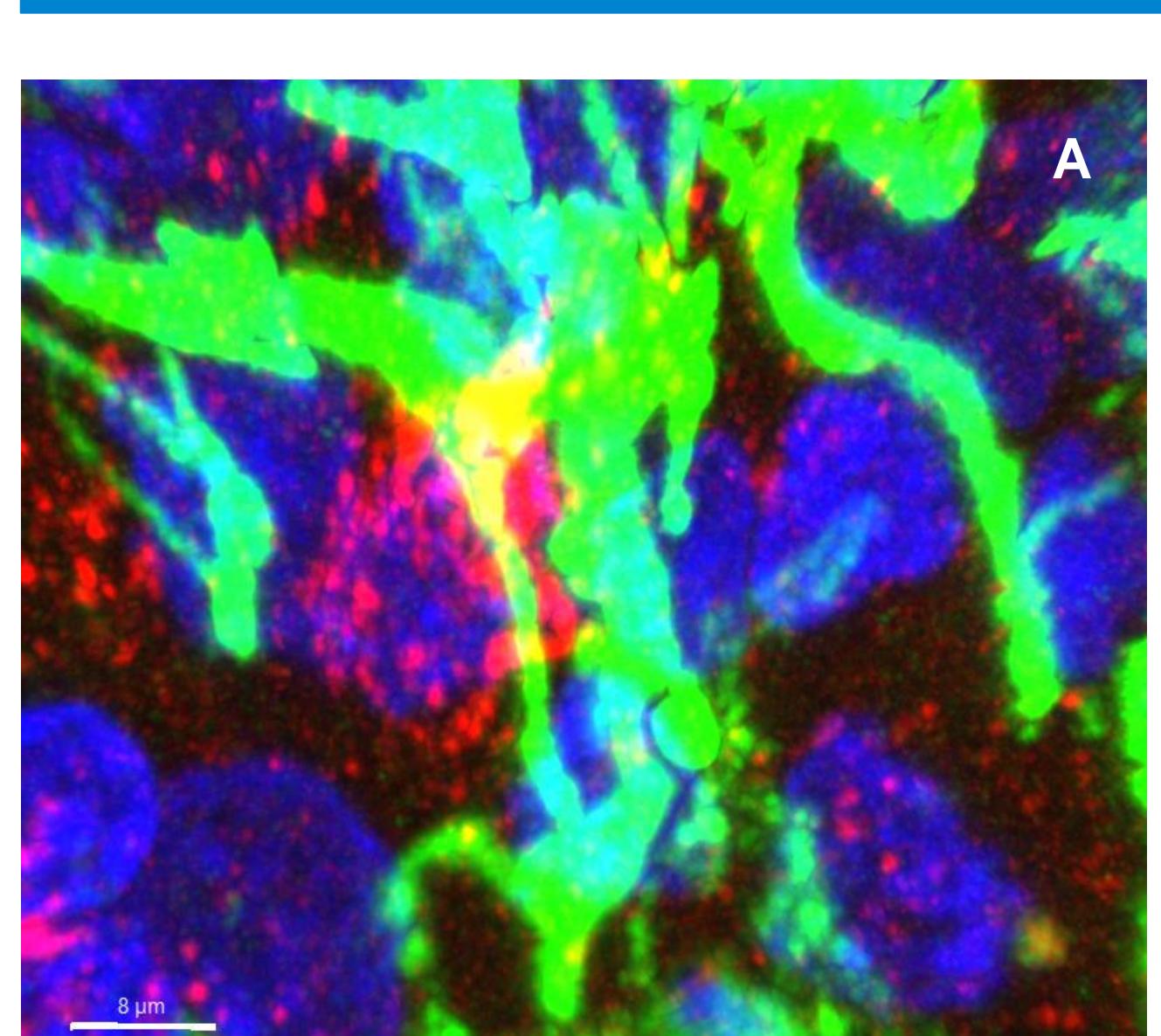
(A) 3D image of a B-cell (red – B-lymphocyte antigen CD20) on actin (green structure). Nuclei are stained in blue (DAPI).
(B) The image shows a 3D reconstructions of the same image.
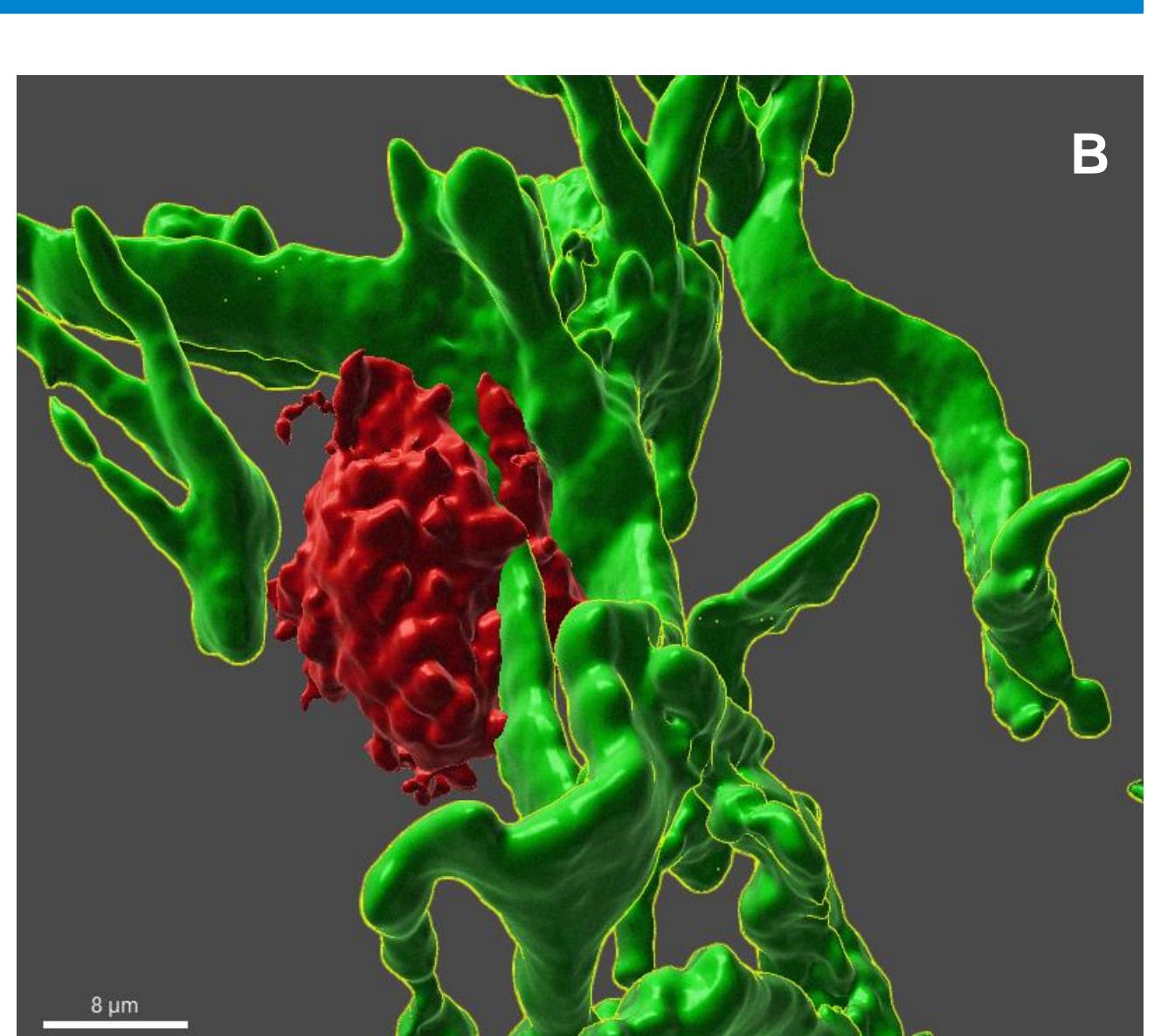
4D
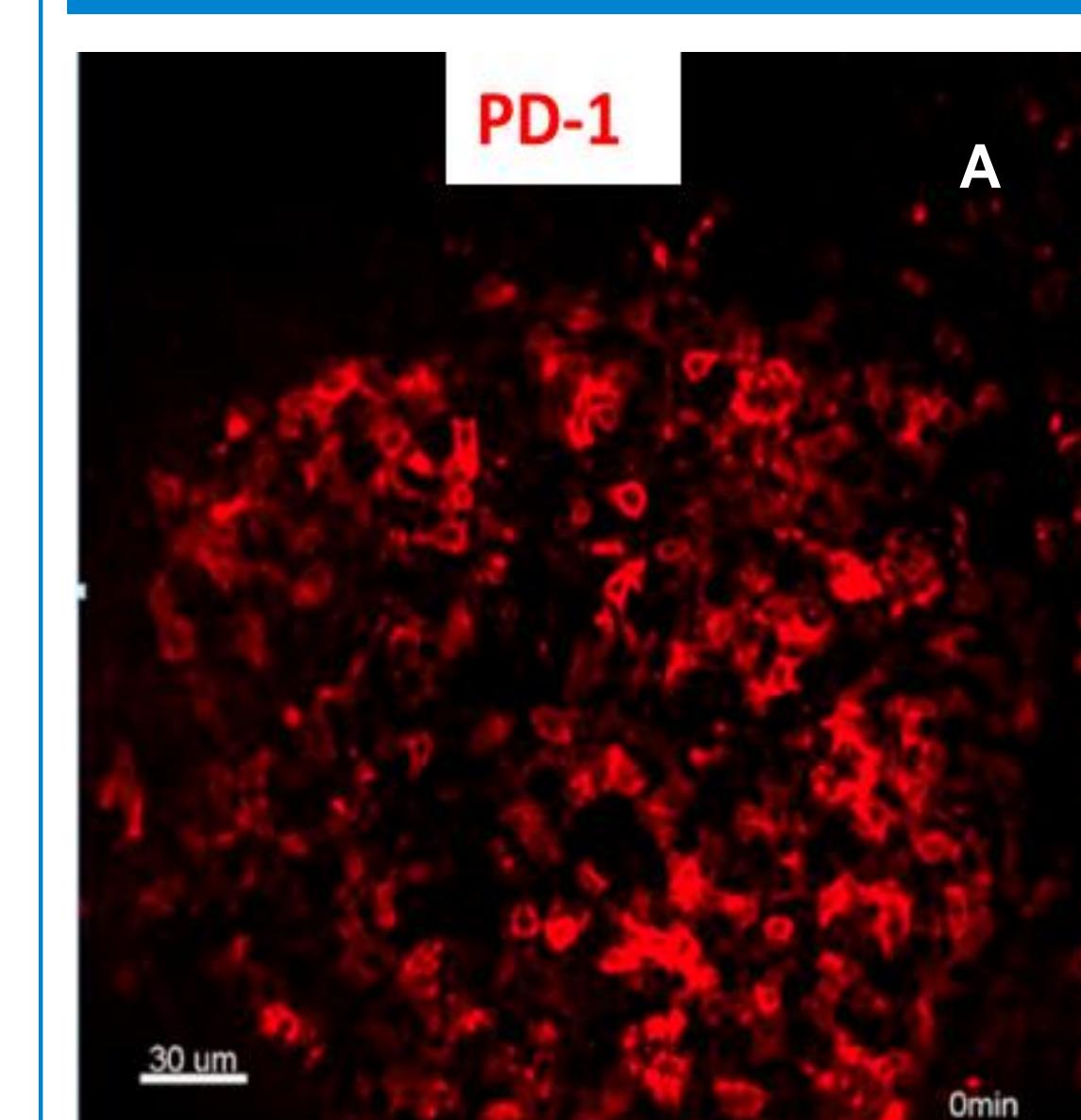
(A) First measurement time point of a 20 min long recording with T follicular helper cells (red – T-lymphocyte antigen PD1) in a human germinal center (GC).
(B) Reconstruction of the distance covered by the T-cells. Tracks are color codes according to PD1 "Track Speed Mean" [3].
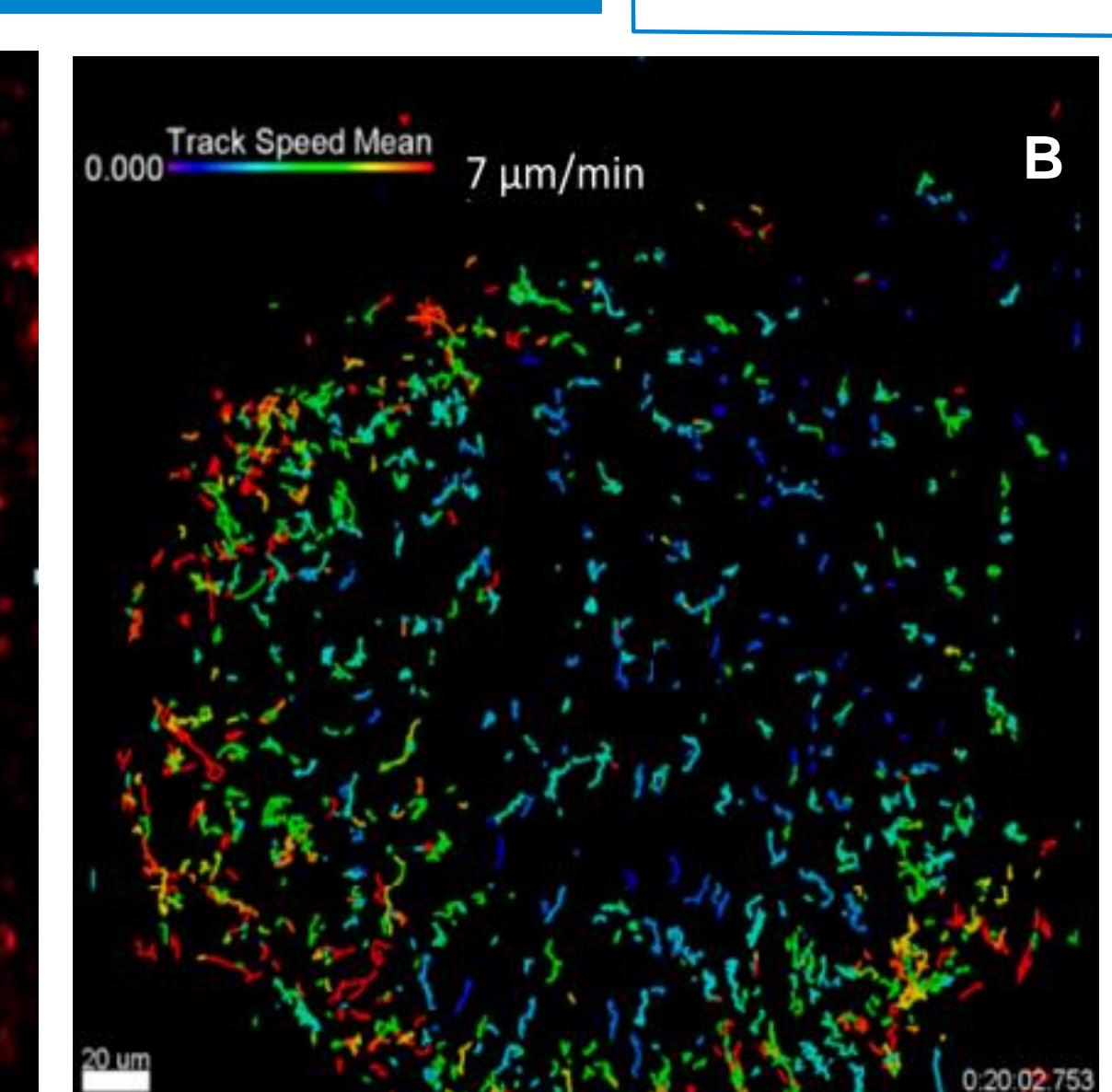
Mathematical model

Model of the lymph node
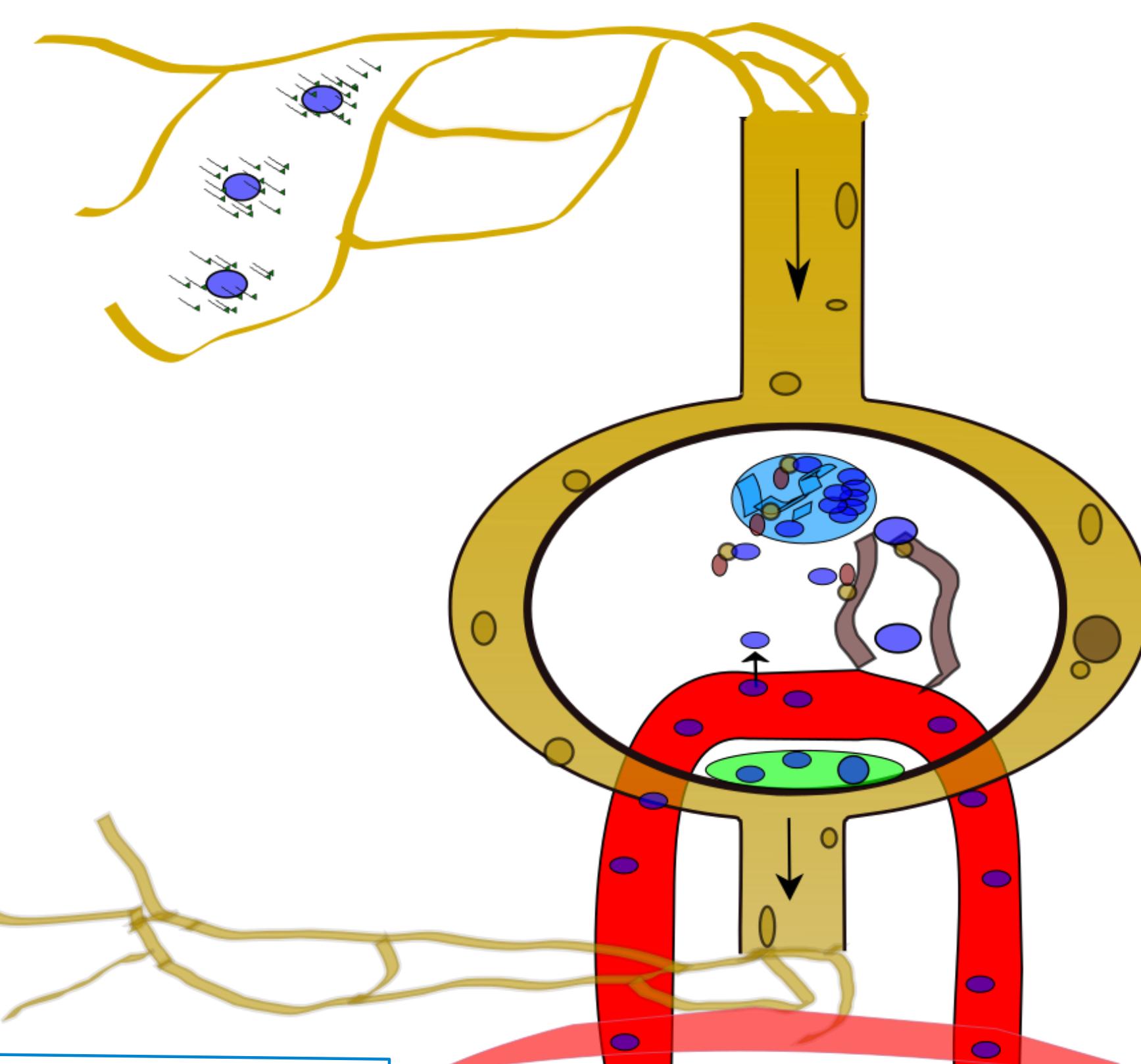
Legend:
- Lymph node
- Antigen
- B-cell
- T-cell
- Germinal center
- Medulla
- Antigen presenting cell
- Blood
- Macrophage

Petri Net of the lymph node
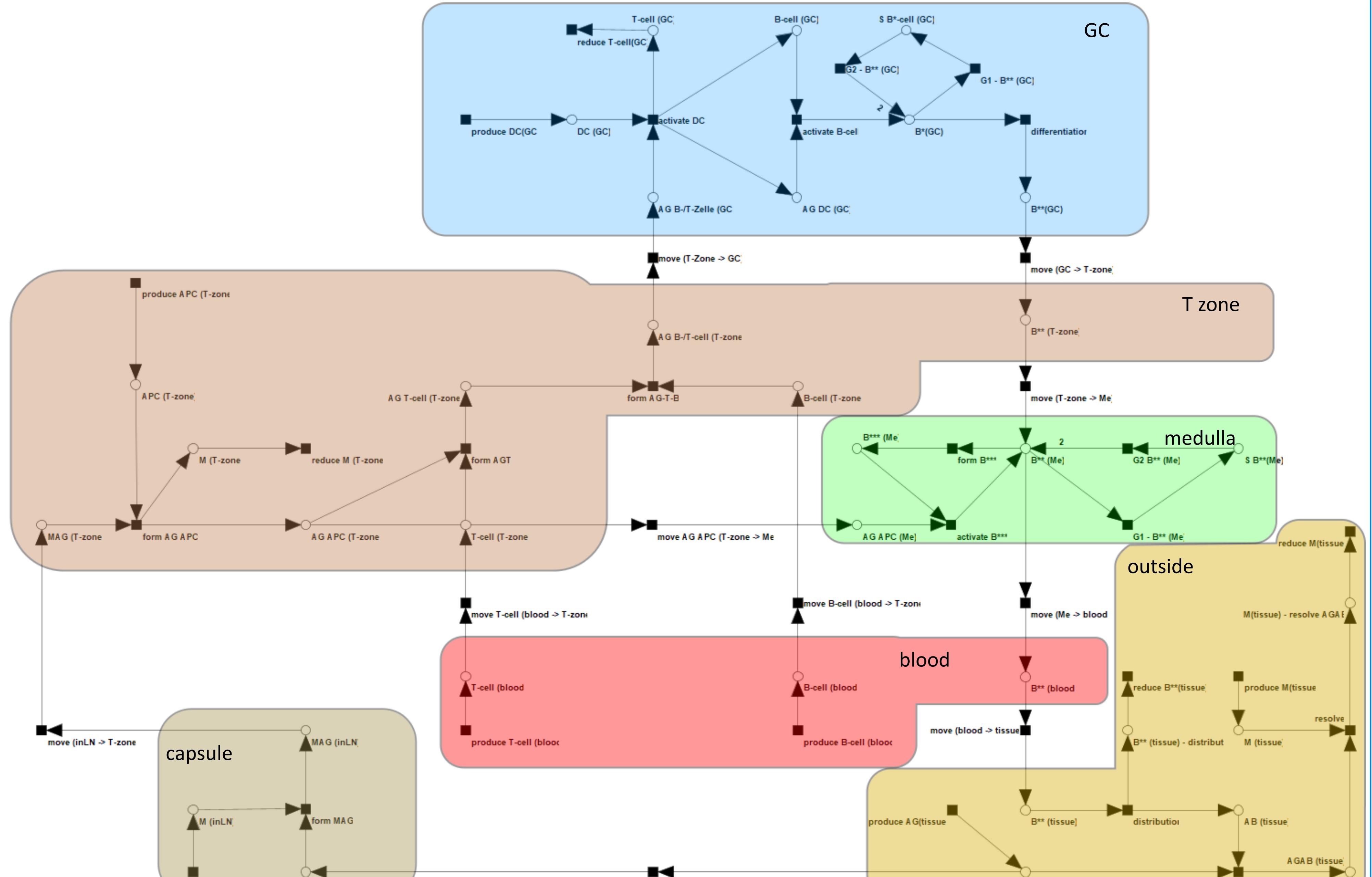
Results:
The PN model describes the processes in different areas of the lymph node. These areas include medulla, germinal center and paracortex. 37 transitions represent cell movements between the zones and the interactions of the different cell types. The 34 places are B-cells, T-cells, macrophages, antigen-presenting cells and dendritic cells. Most of the places are B-cells. The PN model will be extended and improved.

References
[1] Schäfer, Hendrik et al. 2016. Bioinformatics 32(1): 122–29.
[2] Oswald, Marvin et al. 2019. Acta Histochemica 121.
[3] Donnadieu, Emmanuel et al. 2020. The Journal of Immunology
[4] Koch, Ina et al. 2011. Springer, Computational Biology 16.
[5] Balazki, Pavel et al. 2015. BMC Bioinformatics 16(1): 1–11.

FIAS Frankfurt Institute for Advanced Studies   Mol BI