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Mathematical modeling of SARS-CoV-2 infection process and virus spreading in the human body considering B and T cell-mediated immune responses

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In spite of the progress reached in understanding of COVID-19, prediction's fidelity of the development and outcome of the disease still remain deficient. To better understand the progression of COVID-19 patients' clinical picture, molecular mechanisms of interactions between human cells and virus particles taking into account B and T cell-mediated immune responses, a construction of multi-compartmental model considering the specificity of the virus interplay with host cells, its entry and replication, transport throughout tissues and organs, along with formation and development of local and global immune responses to the viral infection, is pivotally required.

We have developed the model, which is based on previously published and tested models of human immune response to Mycobacterium tuberculosis [1] and adaptive B and T cell-mediated immune responses to influenza A virus [2] using a modular modelling approach implemented in open-source software platform BioUML [3]. It incorporates two compartments: lungs and lymph nodes and includes functioning and dynamic of virus, macrophages (resting, activated, infected), dendritic cells (immature and mature), cytotoxic and helper T cells (naïve, Th precursors, Th1 and Tfh), B cells and antibodies (IgA, IgM, IgG), cytokines (IL-4, IL-10, IL-12, IFN-γ) and epithelial cells (infected and uninfected). The model was fitted to the published data on SARS-CoV-2 and it is able to reproduce typical disease progression scenarios, dynamics of T and B cells, and levels of both antibodies and cytokines production as well as the viral load (Fig. 1).

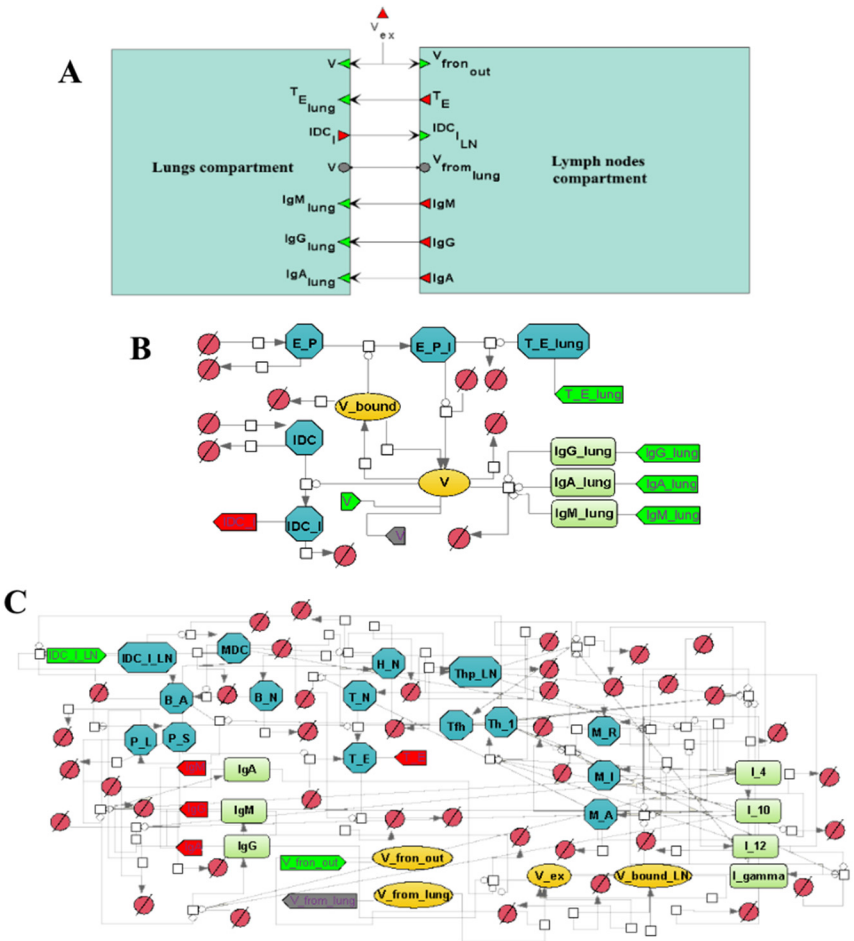

Fig. 1. Model diagrams in BioUML **A)** general composite model; **B**) lungs compartment; **C**) lymph nodes (LN) compartment. E_P – epithelial cells, E_P_I – infected epithelial cells, IDC – immature dendritic cells, MDC – mature dendritic cells, V – virions, Ig – immunoglobulins (G, A, M), B_N – naïve B cells, B_A – activated B cells, P_L – long-lived plasma cells, P_S – short-lived plasma cells, T_N – naïve CD8+ T cells, T_E – CD8+ T cells, H_N – naïve CD4+ T cells, Thp – precursor helper T cells, Th_1 – type 1 helper T cells, Tfh - follicular helper T cells, M_R – resting macrophages, M_I – infected macrophages, M_A – activated macrophages, I – interleukins (4, 10, 12), I_gamma – interferon gamma

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