doi 10.18699/bgrs2024-2.1-20

Modeling iron metabolism in patients with post-COVID syndrome

Melchenko N.I.[1]*, Akberdin I.R.[2]

[1] *Department of Natural Sciences, Novosibirsk State University, Novosibirsk, Russia*

[2] *Department of Computational Biology, Scientific Center for Genetics and Life Sciences, Sirius University of Science and Technology, Sirius, Russia*

* *n.melchenko@g.nsu.ru*

Key words: mathematical model; iron metabolism; post-COVID syndrome; COVID-19

Motivation and Aim: Most patients who have had SARS-CoV-2 infection suffer from nonspecific symptoms for several months, such as fever, headache, attention disorder, hair loss, etc. Analysis of publications and original experimental data shows that some of these symptoms may be related to impaired iron metabolism, since such patients maintain high concentrations of hepcidin and ferritin for a long time and experience iron deficiency [1, 2]. The construction of a mathematical model describing iron metabolism in patients who have suffered the SARS-CoV-2 infection will help one to identify the key mechanisms and limiting factors underlying long-term disturbances in iron metabolism.
Methods and Algorithms: The model is based on previously published models [3, 4] and constructed using ordinary differential equations (ODEs) with a modular approach. BioUML [5] is used as the software for model construction, simulation and analysis. It enables to develop the model according to state-of-the-art systems biology standards, such as SBGN and SBML [6, 7]. In the reproduced Schirm's model we use the proliferation function and Z-function. The latter is used to describe how erythropoietin effects on amplification and transition times in erythroid cells.
Results: We analyzed a number of existing models describing iron metabolism and transport among different human tissues and organs and selected the most promising ones for our research aim. We have completely reproduced the structure of Mitchell's model [3] by modular approach implemented in BioUML (Fig. 1), as well as all the simulation results obtained in the original study (Fig. 2). Furthermore, we have reproduced the Schirm's model structure [4], describing erythropoiesis and the main components of iron metabolism in details, and have already received simulation dynamics describing Z-functions of the amplifications in compartments: burst forming unit erythroid (BE), colony forming unit erythroid (CE) and the transition times in BE and CE.
Conclusion: As an extension of the model of iron metabolism and transport, which takes into account innate and adaptive immune responses, we incorporate into the modular model of iron metabolism and transport modules of the immune response's impact on hepcidin synthesis, iron storage, labile iron concentration, and intestinal iron absorption. The model of iron metabolism in patients with post-Covid syndrome will allow us to better understand the key pathophysiological mechanisms underlying this condition and post-viral syndromes in general. Development of the model that includes two complex systems such as the immune response and iron metabolism can facilitate the further development of more complex models that can describe the functioning of several human organs and systems.

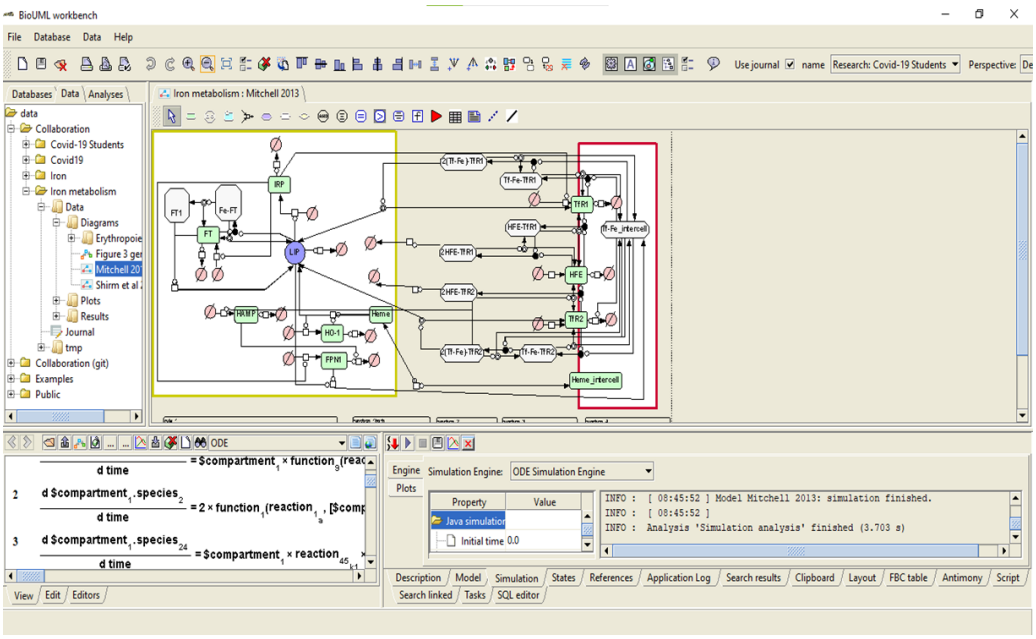

Fig. 1. The modular model of liver iron metabolism reconstructed and analyzed in BioUML from [3]. The compartment with yellow boundary represents the hepatocyte, while the compartment with pink boundary designates plasma. Species overlayed on the compartment boundaries indicate membrane-associated species

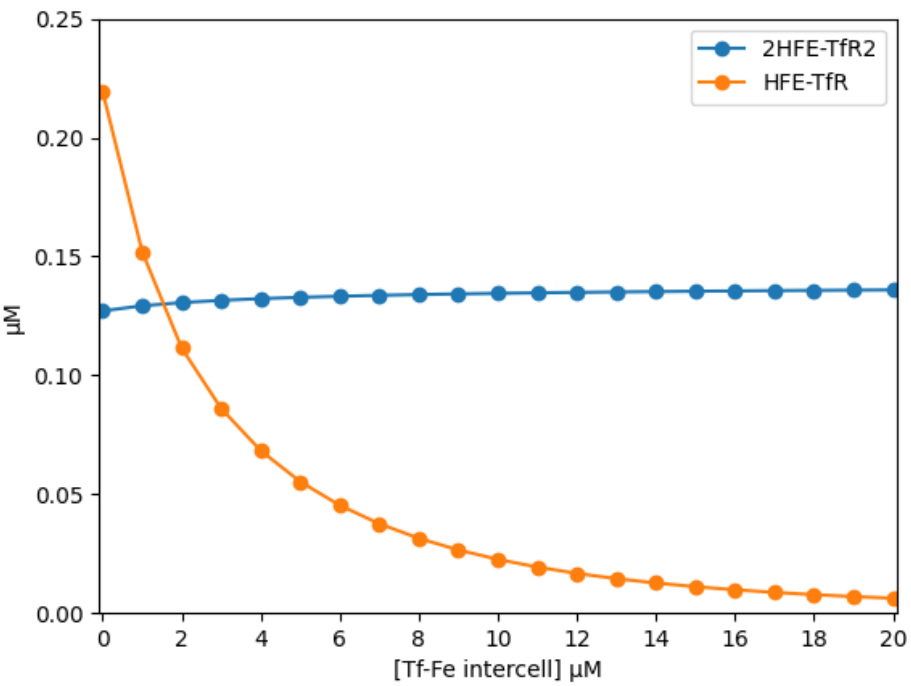

Fig. 2. Reproduced simulation of the steady-state concentrations of metabolites in response to increasing serum Tf-Fe

References

1. Taneri P.E. et al. Anemia and iron metabolism in COVID-19: a systematic review and meta-analysis. *Eur J Epidemiol*. 2020;35(8):763-773. doi 10.1007/s10654-020-00678-5
2. Sonnweber T. et al. The Impact of Iron Dyshomeostasis and Anaemia on Long-Term Pulmonary Recovery and Persisting Symptom Burden after COVID-19: A Prospective Observational Cohort Study. *Metabolites*. 2022;12(6):546. doi 10.3390/metabo12060546
3. Mitchell S., Mendes P.A Computational Model of Liver Iron Metabolism. *PLoS Comput Biol*. 2013;9(11):e1003299. doi 10.1371/journal.pcbi.1003299
4. Schirm S., Scholz M. A biomathematical model of human erythropoiesis and iron metabolism. *Sci Rep*. 2020;10:8602. doi 10.1038/s41598-020-65313-5
5. Kolpakov F. et al. BioUML-towards a universal research platform. *Nucleic Acids Res*. 2022;50(1):124-131. doi 10.1093/nar/gkac286
6. Hucka M. et al. The Systems Biology Markup Language (SBML): Language Specification for Level 3 Version 2 Core Release 2. *J Integr Bioinform*. 2019:16(2):20190021. doi 10.1515/jib-2019-0021
7. Novère N., Hucka M., Mi H. et al. The Systems Biology Graphical Notation. *Nat Biotechnol.* 2009;27:735-741. doi 10.1038/nbt.1558