Open forum

COMMENT ON: "A CRITICAL REVIEW ON HEAT AND MASS TRANSFER MODELLING OF VIRAL INFECTION AND VIRION EVOLUTION The Case of SARS-COV2"

by

Marko E. POPOVIĆ** and Mirjana MINCEVA

Biothermodynamics, TUM School of Life Sciences, Technical University of Munich, Freising, Germany

Original scientific paper
https://doi.org/10.2298/TSCI211021329P

In the journal *Thermal Science*, Year 2021, Volume 25, Issue 4, pp. 2831-2843, a paper was published by Trancossi *et al*., entitled *A critical review on heat and mass transfer modelling of viral infection and virion evolution: The case of SARS-CoV2*, [1]. This paper, using SARS-CoV-2 as an example, analyses viral infection and evolution.

At several places in the paper [1], papers by Popovic and Minceva are cited, entitled *A Thermodynamic Insight into Viral Infections: Do Viruses in a Lytic Cycle Hijack Cell Metabolism due to their Low Gibbs Energy?* [2] and *Thermodynamic Insight into Viral Infections 2: Empirical Formulas, Molecular Compositions and Thermodynamic Properties of SARS, MERS and SARS-Cov-2 (COVID-19) Viruses* [3], as well as *Thermodynamic Properties of Human Tissues* [4]. Moreover, papers by Popović are cited: *Thermodynamic Properties of Microorganisms: Determination and Analysis of Enthalpy, Entropy, and Gibbs Free Energy of Biomass, Cells and Colonies of 32 Microorganism Species* [5], *Entropy Change of Open Thermodynamic Systems in Self-Organizing Processes* [6].

In their paper, Trancossi *et al*. [1], have misinterpreted the papers by Popović and Minceva [2020a, 2020b], claiming that equilibrium thermodynamics is used. For example, *According to a traditional equilibrium thermodynamic model, Popovic and Minceva [1] have proposed an excellent bio-thermodynamic analysis of MERS-CoV, SARS-CoV, and SARS-CoV-2.* [Trancossi *et al*., 2021, p. 2831]. However, a non-equilibrium thermodynamic model has been used in the cited papers [2, 3], based on linear phenomenological equations. The linear phenomenological equation relates the rate of a process, r, and its Gibbs energy change, $\Delta_r G$

$$r = -\frac{L}{T}\Delta_r G \tag{1}$$

where T is the temperature and L is the phenomenological coefficient, a constant specific for the process.

Trancossi *et al*. wrote *The outstanding work by Popovich and Minceva [1-4] move in the frame of traditional thermodynamics of closed systems*. [Trancossi *et al*., 2021, p.

*Corresponding author, e-mail: marko.popovic@tum.de

2834]. However, in the papers [2-5], microorganisms were clearly stated to be open thermodynamic systems and hence non-equilibrium thermodynamics should be used to analyse them.

Phenomenological equations are an important part of non-equilibrium thermodynamics and are often used to analyze non-equilibrium processes [7]. Equation (1) says that chemical reaction rate is proportional to its driving force – the reaction Gibbs energy [7]. The greater the reaction Gibbs energy, the faster the reaction becomes. On the other hand, at equilibrium, reaction Gibbs energy becomes zero $\Delta_r G = 0$ [7, 8]. Thus, the reaction rate also becomes zero, $r = 0$. This corresponds to the observation that reactions cease once they reach chemical equilibrium.

Both papers by Popović and Minceva [2, 3] dealing with viral multiplication use the phenomenological eq. (1) and hence the non-equilibrium thermodynamic approach to analyse the phenomenon of growth. Moreover, growth is analysed by Popović and Minceva [2, 3] as an irreversible process out of equilibrium. This confirms the misinterpretation published in the paper by Trancossi *et al*. [1].

Another issue that drew our attention was lack of citation for the atom counting method for determining virus elemental composition. The atom counting method for determining elemental composition of viruses is suggested in Popović and Minceva [2, 3]. However, Trancossi *et al*. [1] write … *the four main components of viruses: nucleic acids, proteins, lipids, and non-nucleic acid carbohydrates. They have well-defined elemental composition and allow determining the elemental composition of virions by the atom counting method. In the virion, the total number of atoms of the element J is the sum of contributions from four classes of molecules:* $N_{J,virus} = N_{J,NA} + N_{J,prot} + N_{J,lip} + N_{J,CH}$ [Trancossi *et al*., 2021, p. 2833]. In this paragraph, the source of the atom counting method is not cited. The atom counting method was suggested in [3].

Similarly, the method for determining elemental composition of lipids also lacks a citation. Trancossi *et al*. wrote *The number of lipid molecules can be determined by accounting for the free volume between envelope proteins… The number of lipid constituent X, c(X), was determined by multiplying Clip with the mole fraction of that lipid, x(X): c(X) = x(X) Clip (2). The number element J atoms in all lipids,* $N_{J,lip}$*, was determined:* $N_{J,lip} = \Sigma_X n_{J,X} C_X$ *(3) where* $n_{J,X}$ *is the number of atoms of element J in a single molecule of the lipid X*. [Trancossi *et al*., 2021, p. 2833] without citing the source of the method. This method for determining elemental composition of virus lipids was previously published in [3].

This reply to the paper by Trancossi *et al*. [1] focuses only on the noticed misinterpretation of the papers by Popović and Minceva [2, 3]. The focus of this reply is not to criticize the conclusions of Trancossi *et al*. [1].

Reference

[1] Trancossi, M., *et al*., A Critical Review on Heat and Mass Transfer Modelling of Viral Infection and Virion Evolution: The Case of SARS-CoV2, *Thermal Science, 25* (2021), 4A, pp. 2831-2843
[2] Popović, M. E., Minceva, M., A Thermodynamic Insight Into Viral Infections: Do Viruses in a Lytic Cycle Hijack Cell Metabolism Due to Their Low Gibbs Energy?. *Heliyon, 6* (2020), 5, e03933
[3] Popović, M. E., Minceva, M., Thermodynamic Insight Into Viral Infections 2: Empirical Formulas, Molecular Compositions and Thermodynamic Properties of SARS, MERS and SARS-CoV-2 (COVID-19) Viruses. *Heliyon, 6* (2020), 9, e04943
[4] Popović, M. E., Minceva, M., Thermodynamic Properties of Human Tissues, *Thermal Science, 24* (2020), 6B, pp. 4115-4133
[5] Popovic, M. E., Thermodynamic Properties of Microorganisms: Determination and Analysis of Enthalpy, Entropy, and Gibbs Free Energy of Biomass, Cells and Colonies of 32 Microorganism Species, *Heliyon , 5* (2019), 6, e01950

[6] Popovic, M. E., Entropy Change of Open Thermodynamic Systems in Self-Organizing Processes. *Thermal Science*, *18* (2014), 4, pp. 1425-1432
[7] Demirel, Y., *Nonequilibrium Thermodynamics: Transport and Rate Processes in Physical, Chemical and Biological Systems*, 3rd ed., Elsevier, Amsterdam, The Netherlands, 2014
[8] Atkins, P., de Paula, J., *Physical Chemistry for the Life Sciences*, 2nd ed., W. H. Freeman and Company, New York, USA, 2011

Paper accepted: October 21, 2021