10th World Congress on
Physical and Theoretical Chemistry
October 20-21, 2022 | Webinar
Volume: 12

SARS-CoV-2 Main Protease: A Kinetic Approach

Thierry Rebetez

Department of Sciences, Institute of Biology, University of Neuchâtel, Neuchâtel, Switzerland.

Background: In this article, I present a new model of the interaction of the main protease (Mpro) from SARS-CoV-2 virus with its substrate. The reaction scheme used to describe this mechanism is an extension of the well-known Michaelis-Menten model proposed in 1913 by Leonor Michaelis and Maud Menten. The model I present here takes into account that one Mpro enzyme monomer interacts with another Mpro monomer in the presence of the substrate, leading to the formation of an enzyme dimer bound to one substrate molecule. This reaction mechanism is also known in the literature as substrate-induced dimerization.

Methods: Starting from this new reaction scheme, I derived a mathematical expression describing the catalytic rate of the active Mpro enzyme dimer as a function of the substrate concentration. Furthermore, I wanted to see if this catalytic behavior was also observed in vitro. Therefore, I measured the catalytic rate of the Mpro dimer for different substrate concentrations. The properties of my substrate construct were such that I could determine the catalytic rate of the enzyme dimer by directly measuring the spectrophotometric absorbance of the cleaved substrate at 405 nm.

Results: On the plot corresponding to this reaction, at the time where the reaction rate begins to decrease, we observe a new phenomenon that appears: The enzyme monomers begin to be "diluted" in the solution containing the excess substrate. The dimers begin to dissociate and bind increasingly to the substrate as inactive monomers instead of active dimers. Hence, it is more and more unlikely for the enzyme monomers to sequentially bind twice to the same substrate molecule. Furthermore, I have determined Vmax and SVmax numerically. Moreover, I have established that the maximum of the fitted curve depends only on the total enzyme concentration and not on the concentration of substrate.

Conclusion: The results show explicitly-within a margin of error-that the overall shape of the experimental curve looks like the one of the theoretical curve. This finding could open new doors in the discovery of drugs directed against the Mpro enzyme of the SARS-CoV-2 virus, acting on the inhibition of the Mpro enzyme by excess-substrate.

Biography:

Thierry Rebetez works in the Department of Sciences, Institute of Biology, University of Neuchâtel, Neuchâtel, Switzerland.

thierry.rebetez@gmail.com