

# Mathematical modeling of the relocation of the divalent metal transporter DMT1 in the intestinal iron absorption process

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Iron is essential for the normal development of cellular processes. This metal has a high redox potential that can damage cells and its overload or deficiency is related to several diseases, therefore it is crucial for its absorption to be highly regulated. A fast-response regulatory mechanism has been reported known as mucosal block, which allows to regulate iron absorption after an initial iron challenge. In this mechanism, the internalization of the DMT1 transporters in enterocytes would be a key factor. Two phenomenological models are proposed for the iron absorption process: DMT1's binary switching mechanism model and DMT1's swinging-mechanism model, which represent the absorption mechanism for iron uptake in intestinal cells. The first model considers mutually excluding processes for endocytosis and exocytosis of DMT1. The second model considers a Ball's oscillator to represent the oscillatory behavior of DMT1's internalization. Both models are capable of capturing the kinetics of iron absorption and represent empirical observations, but the DMT1's swingingmechanism model exhibits a better correlation with experimental data and is able to capture the regulatory phenomenon of mucosal block. The DMT1 swinging-mechanism model is the first phenomenological model reported to effectively represent the complexity of the iron absorption process, as it can predict the behavior of iron absorption fluxes after challenging cells with an initial dose of iron, and the reduction in iron uptake observed as a result of mucosal block after a second iron dose.