

In Silico Methods for Assessing the Compounds' Permeability Through the Blood-Brain Barrier

Nicoleta Siminea^{1,2,*}, Andrei Păun^{1,2,3}, Ion Petre^{2,4}

¹ Faculty of Mathematics and Computer Science, University of Bucharest, Bucharest, Romania

² National Institute of Research and Development for Biological Sciences, Bucharest, Romania

³ Research Institute for Artificial Intelligence (ICIA), Romanian Academy, Bucharest

⁴ Department of Mathematics and Statistics, University of Turku, Finland

* Correspondence: insae@univ-ovidius.ro;

Received: 7.08.2025; Accepted: 21.09.2025; Published: 16.11.2025

Abstract: In the development of novel treatments for various diseases, a critical step involves the ability of active compounds to pass through the blood-brain barrier. The underlying motivation stems from the dual perspective that sometimes it is undesirable for compounds to cross the barrier, while in other cases, it is beneficial for them to do so in substantial amounts. This duality is based on the fact that these compounds can be toxic to the central nervous system or, conversely, can be effective in treating brain diseases. It is well known that, historically, negative results regarding blood-brain barrier permeability have led to the halting of research into potential treatments for the central nervous system. Recent advances in biotechnology are helping to overcome this shortcoming, but unfortunately, the cost of production is also increasing. Therefore, even in the case of these substances, determining whether a substance crosses the blood-brain barrier is essential for subsequent management. Given the excessive costs and time requirements associated with experimental testing — especially when evaluating a broad spectrum of compounds — in silico computational methods have been developed to streamline the screening process. As a large proportion of them consists of machine learning models, our aim was to offer a comprehensive overview of the models that can be used to determine this important property of a compound, the key features these models rely on, and the challenges that may be encountered when applying them.

Keywords: Blood-Brain Barrier; In Silico Screening; Machine Learning Models; CNS Drug Development; Permeability Prediction.

© 2025 by the authors. This article is an open-access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited. The authors retain copyright of their work, and no permission is required from the authors or the publisher to reuse or distribute this article, as long as proper attribution is given to the original source.