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BOOK OF ABSTRACTS OF THE 8TH MEETING ON MEDICINAL BIOTECHNOLOGY

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Evaluation of Deep Learning Models for Aptamer Modelling In Silico

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Aptamers are single-stranded DNA or RNA oligonucleotides that fold into complex three-dimensional structures to bind molecular targets with high affinity and specificity (1). Often termed "chemical antibodies," these biomaterials are vital for diverse applications in therapeutics, diagnostics, bioassays, and in vitro and in vivo imaging (2). Historically, aptamer discovery has relied on the Systematic Evolution of Ligands by EXponential Enrichment (SELEX), an in vitro process involving iterative selection, amplification and enrichment rounds. However, SELEX is time-consuming and often results in low success rates (3). Consequently, an *in silico* approach is essential to streamline the discovery process, reduce experimental costs, and provide insights into aptamer-target interactions. Recently, various deep learning models capable of predicting the 3d structure of aptamer-target complexes have become available. In this work, we evaluated general biomolecular prediction models, like Alphafold-3, Protenix-v2, Chai-1, Boltz-2, Openfold-3, RoseTTAFold2NA, and two specialized aptamer modelling tools, AptaTrans and AptaBLE. Among the evaluated models, AlphaFold-3 stands as the current state-of-the-art general model for aptamer modelling, with Protenix-v2, Chai-1, Boltz-2 and RoseTTAFold2NA, accuracies falling short of AlphaFold-3. The only model that rivals Alphafold-3 in aptamer-target benchmarks is OpenFold-3. On the other hand, specialized tools such as AptaTrans and AptaBLE, significantly outperform AlphaFold3 on validated DNA and RNA aptamers, which can be attributed to their optimization for sequence-based patterns. Overall, this work highlights the importance of an *in silico* approach for aptamer discovery and evaluates deep learning models capable of predicting the 3D structure of aptamer-target complexes. While general models provide a robust baseline for aptamer-target complex structure prediction, specialized tools offer enhanced performance for aptamer discovery. Future work will include a systematic comparison of the evaluated models.

KEYWORDS: *aptamers*, *deep learning*, *in silico*

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