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Prediction of Asp Deamidation Propensity in Proteins by Physical-based Descriptors

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The development process of biotherapeutic products faces remarkable challenges in identifying novel, effective and safe candidates, with chemical stability emerging as a critical obstacle that hinders the discovery process. Among chemical instabilities, the occurrence of spontaneous chemical reactions, known as Post-

Translational Modifications (PTMs), emerge as a crucial factor during the development process.

Here, we present a theoretical-computational approach able to provide a molecular understanding beyond one of the most common chemical instabilities, the spontaneous deamidation of Asparagine residues in proteins.

For this purpose, we have designed a set of structural-dynamics parameters, estimated by long timescale MD simulations, with the aim of capturing the molecular basis of Asn reactivity. The capability of the designed parameters

to discriminate Asn susceptibility was then assessed by employing Machine Learning algorithms. The satisfactory prediction metrics obtained demonstrate that an accurate selection of features, based on the physical-chemical behaviour of the residues, might play a pivotal role in the high throughput screening of biotherapeutics in the early stage of development.