Parnet: a protein–RNA interaction–based RNA foundation model for functional prediction and therapeutic design

Annalisa Marsico1 1Computational Health Center, Helmholtz Center Munich, Munich, Germany

Background: RNA-binding proteins (RBPs) are central regulators of post-transcriptional gene expression, controlling processes such as splicing, mRNA stability and translation. Computational analysis of high-resolution CLIP-seq data has enabled mapping of RBP binding sites and the cis-regulatory elements that govern these interactions, while also providing the foundation for AI models that can predict RNA–protein interactions in contexts where experimental data are unavailable. More recently, the field has shifted from specialized task-specific models toward RNA foundation models—selfsupervised models trained on vast collections of unlabeled RNA sequences—that enable more holistic representations of RNA function and support in silico hypothesis generation. Method: Building on the premise that RNA function is encoded in its interaction partners, we developed Parnet, a multi-task model that densely represents the RNA interactome. Extending our earlier single-task model RBPNet, Parnet is trained end-to-end on raw CLIP-seq profiles from hundreds of RBPs to predict genome-wide binding profiles directly from sequence. In contrast to unsupervised RNA language models, Parnet learns embeddings that capture the combinatorial “RBP code” underlying post-transcriptional regulation and yield transferable functional representations that support a wide range of downstream predictive tasks. Results: As a result, Parnet generalizes across downstream tasks—including splicing prediction, identification of intron retention events, mRNA translation and scoring of clinical non-coding variants—often with minimal or no fine-tuning, and enables mechanistic interpretation of predictions. In a therapeutic context, we show the potential of Parnet to computationally prioritize functional Antisense Oligonucleotide hotspots in concrete applications and to design mRNA UTRs that achieve desired expression, stability, and regulatory profiles. Conclusion: Together, these results establish Parnet as a foundation model of the RNA interactome, providing transferable representations that enable both biological discovery and RNA therapeutic design.