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RNA secondary structures scale as self-avoiding randomly branched polymers

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Ribonucleic acid (RNA) is a heteropolymer of four nucleotides (A, C, G, and U) which interact and form different base pairs with each other. Base pairing bewteen nucleotides in an RNA sequence gives rise to a secondary structure where base-paired (double-stranded) helices are interspersed with stretches of unpaired (single-stranded) nucleotides. In long RNA sequences, this leads to formation of complex structures with branching architectures, whose topology often comes with functional consequences such as increased compactness or enhanced interactions with the environment. When RNA secondary structures are mapped to mathematical trees, the structures and their topology can be analyzed within the framework of the statistical physics of branched polymers. I will show that a Flory-type analysis applied to the topological properties of RNA structure results in characteristic scaling exponents that are similar to those of self-avoiding randomly branched polymers in two and three dimensions. This result is surprising as the prediction of RNA secondary structure depends solely on the nearest-neighbour energies of base pair formation and does not include any steric interactions, which otherwise distinguish self-avoiding and ideal polymers. Furthermore, I will demonstrate that the scaling behaviour of RNA structures is robust across different sequence compositions and energy models, persisting down to the most bare-bones models of secondary structure. Only if the actual tree topologies are shuffled does one obtain the scaling exponents characteristic of ideal branched polymers. Put differently, the topologies of RNA secondary structures consistently assume only a specific subset of all possible tree topologies in a way that makes their scaling behaviour similar to the one of self-avoiding branched polymers. Our work explores the conditions under which this remains true as well as in what way the scaling properties are encoded in the sequence and structure of RNA.

[1] D. Vaupotič et al., *arXiv preprint*, arXiv:2409.16007 [cond-mat.soft] (2024).
[2] D. Vaupotič et al., *J. Chem. Phys.* **158**, 234901 (2023).

Author: BOZIC, Anze (Department of Theoretical Physics, Jozef Stefan Institute)

Co-authors: Dr ROSA, Angelo (SISSA); VAUPOTIČ, Domen; Dr MORAND, Jules (University of Trento); Prof. TUBIANA, Luca (University of Trento, Italy)

Presenter: BOZIC, Anze (Department of Theoretical Physics, Jozef Stefan Institute)