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**The ribosome as an optimal decoder: a lesson in molecular recognition** TSVI TLUSTY, Institute for Advanced Study, Princeton, YONATAN SAVIR, Harvard Medical School, Systems Biology — The ribosome is a complex molecular machine that, in order to synthesize proteins, has to decode mRNAs by pairing their codons with matching tRNAs. Decoding is a major determinant of fitness and requires accurate and fast selection of correct tRNAs among many similar competitors. However, it is unclear whether the present ribosome, and in particular its large deformations during decoding, are the outcome of adaptation to its task as a decoder or the result of other constraints. Here, we derive the energy landscape that provides optimal discrimination between competing substrates, and thereby optimal tRNA decoding. We show that the measured landscape of the prokaryotic ribosome is indeed sculpted in this way. This suggests that conformational changes of the ribosome and tRNA during decoding are means to obtain an optimal decoder. Our analysis puts forward a generic mechanism that may be utilized by other ribosomes and other molecular recognition systems.

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