

# Single molecule derivation of base pair free energies in DNA and RNA

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Recent developments in micro and nano-technologies allow for the controlled manipulation of individual molecules by exerting and detecting forces in the piconewton range<sup>1</sup>. Molecular unzipping is a force-induced reaction that makes possible to disrupt the bonds that hold molecular structures in nucleic acids and proteins. In this way, for example, a double stranded DNA molecule can be converted into two individual single strands by pulling apart the two strands (molecular unzipping)<sup>2</sup>. The capability of single molecule techniques of detecting weak forces together with the ability of measuring extensions with nanometer resolution allow scientists to monitor molecular reactions in real time (e.g. molecular folding). In this communication we will show some of the most recent applications of molecular unzipping in our lab that make possible to derive base-pair free energies in DNA and RNA with unprecedented accuracy and extract folding free energies of proteins with

1kcal/mol resolution<sup>3,4</sup>.

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<sup>1</sup> F. Ritort, Single molecule experiments in biological physics: methods and applications, *Journal of Physics C (Condensed Matter)*, 18 (2006) R531-R583

<sup>2</sup> N. Forns, S. De Lorenzo, M. Manosas, K. Hayashi, J. M. Huguet and F. Ritort, Improving Signal/Noise Resolution in Single-Molecule Experiments Using Molecular Constructs with Short Handles, *Biophysical Journal*, 100 (2011) 1765-1774

<sup>3</sup> J. M. Huguet, C. V. Bizarro, N. Forns, S. B. Smith, C. Bustamante and F. Ritort, Single-molecule derivation of salt dependent base-pair free energies in DNA, *Proceedings of the National Academy of Sciences*, 107 (2010) 15431-15436

<sup>4</sup> C. V. Bizarro, A. Alemany, F. Ritort. Non-specific binding of Na<sup>+</sup> and Mg<sup>2+</sup> to RNA determined by force spectroscopy methods, *Nucleic Acids Res.*, 2012