

VU Research Portal

Acoustic Force Spectroscopy (AFS)

Kamsma, D.

2018

document version

Publisher's PDF, also known as Version of record

[Link to publication in VU Research Portal](#)

citation for published version (APA)

Kamsma, D. (2018). *Acoustic Force Spectroscopy (AFS): From single molecules to single cells*.

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal ?

Take down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

E-mail address:

vuresearchportal.ub@vu.nl

References

1. Marco Dorigo, Mauro Birattari, T. S. Ant Colony Optimization . A Computational Intelligence Technique. *IEEE Comput. Intell. Mag.* **1**, 28–39 (2006).
2. Rickles, D., Hawe, P. & Shiell, A. A simple guide to chaos and complexity. *J. Epidemiol. Community Heal.* **61**, 933–937 (2007).
3. Sweetlove, L. Number of species on Earth tagged at 8.7 million. *Nat. Online* (2011).
4. Alberts, B. *et al. Molecular Biology of the Cell.* (Garland Science;, 2007).
5. Kim, M.-S. *et al.* A draft map of the human proteome. *Nature* **509**, 575–581 (2014).
6. Milo, R. What is the total number of protein molecules per cell volume? A call to rethink some published values. *BioEssays* **35**, 1050–1055 (2013).
7. Huang, B., Bates, M. & Zhuang, X. Super resolution fluorescence microscopy. *Annu. Rev. Biochem.* **78**, 993–1016 (2010).
8. Bustamante, C., Cheng, W. & Mejia, Y. X. Revisiting the Central Dogma One Molecule at a Time. *Cell* **144**, 480–497 (2011).
9. Neuman, K. K. C. & Nagy, A. Single-molecule force spectroscopy: optical tweezers, magnetic tweezers and atomic force microscopy. *Nat. Methods* **5**, 491–505 (2008).
10. Herbert, K. M., Greenleaf, W. J. & Block, S. M. Single-Molecule Studies of RNA Polymerase: Motoring Along. *Annu. Rev. Biochem.* **77**, 149–176 (2008).
11. Zhao, Y. *et al.* Lab-on-a-chip technologies for single-molecule studies. *Lab Chip* **13**, 2183–98 (2013).
12. De Vlamincq, I. & Dekker, C. Recent Advances in Magnetic Tweezers. *Annu. Rev. Biophys.* **41**, 453–472 (2012).
13. Kim, S., Blainey, P. C., Schroeder, C. M. & Xie, X. S. Multiplexed single-molecule assay for enzymatic activity on flow-stretched DNA. *Nat. Methods* **4**, 397–399 (2007).
14. Halvorsen, K. & Wong, W. P. Massively parallel single-molecule manipulation using centrifugal force. *Biophys. J.* **98**, L53-5 (2010).
15. Fazio, T., Visnapuu, M.-L., Wind, S. & Greene, E. C. DNA curtains and nanoscale curtain rods: high-throughput tools for single molecule imaging. *Langmuir* **24**, 10524–31 (2008).
16. Smith, S. B., Cui, Y. & Bustamante, C. Overstretching B-DNA: The Elastic Response of Individual Double-Stranded and Single-Stranded DNA Molecules. *Science (80-.).* **271**, 795–799 (1996).
17. van Mameren, J. *et al.* Unraveling the structure of DNA during overstretching by using multicolor, single-molecule fluorescence imaging. *Proc. Natl. Acad. Sci. U. S. A.* **106**, 18231–6 (2009).
18. Settnes, M. & Bruus, H. Forces acting on a small particle in an acoustical field in a viscous fluid. *Phys. Rev. E - Stat. Nonlinear, Soft Matter Phys.* **85**, 1–12 (2012).
19. Heller, I. *et al.* STED nanoscopy combined with optical tweezers reveals protein dynamics on densely covered DNA. *Nat. Methods* **10**, 910–916 (2013).

20. Glynn-Jones, P., Boltryk, R. J. & Hill, M. Acoustofluidics 9: Modelling and applications of planar resonant devices for acoustic particle manipulation. *Lab Chip* **12**, 1417 (2012).
21. Laurens, N. *et al.* Dissecting protein-induced DNA looping dynamics in real time. *Nucleic Acids Res.* **37**, 5454–5464 (2009).
22. Odijk, T. Stiff Chains and Filaments under Tension. *Macromolecules* **28**, 7016–7018 (1995).
23. Chen, Z., Yang, H. & Pavletich, N. P. Mechanism of homologous recombination from the RecA-ssDNA/dsDNA structures. *Nature* **453**, 489–4 (2008).
24. Fu, H., Le, S., Muniyappa, K. & Yan, J. Dynamics and Regulation of RecA Polymerization and De-Polymerization on Double-Stranded DNA. *PLoS One* **8**, e66712 (2013).
25. Merkel, R., Nassoy, P., Leung, a, Ritchie, K. & Evans, E. Energy landscapes of receptor-ligand bonds explored with dynamic force spectroscopy. *Nature* **397**, 50–3 (1999).
26. Neuert, G., Albrecht, C., Pamir, E. & Gaub, H. E. Dynamic force spectroscopy of the digoxigenin-antibody complex. *FEBS Lett.* **580**, 505–509 (2006).
27. Moayed, F., Mashaghi, A. & Tans, S. J. A polypeptide-DNA hybrid with selective linking capability applied to single molecule nano-mechanical measurements using optical tweezers. *PLoS One* **8**, e54440 (2013).
28. Hill, M., Shen, Y. & Hawkes, J. J. Modelling of layered resonators for ultrasonic separation. *Ultrasonics* **40**, 385–392 (2002).
29. Hill, M., Townsend, R. J. & Harris, N. R. Modelling for the robust design of layered resonators for ultrasonic particle manipulation. *Ultrasonics* **48**, 521–528 (2008).
30. Gosse, C. & Croquette, V. Magnetic Tweezers: Micromanipulation and Force Measurement at the Molecular Level. *Biophys. J.* **82**, 3314–3329 (2002).
31. te Velthuis, A. J. W., Kerssemakers, J. W. J., Lipfert, J. & Dekker, N. H. Quantitative guidelines for force calibration through spectral analysis of magnetic tweezers data. *Biophys. J.* **99**, 1292–1302 (2010).
32. Berg-Sørensen, K. & Flyvbjerg, H. Power spectrum analysis for optical tweezers. *Rev. Sci. Instrum.* **75**, 594–612 (2004).
33. Schäffet, E., Nørrelykke, S. F. & Howard, J. Surface forces and drag coefficients of microspheres near a plane surface measured with optical tweezers. *Langmuir* **23**, 3654–3665 (2007).
34. Norrelykke, S. F. & Flyvbjerg, H. Power spectrum analysis with least-squares fitting: Amplitude bias and its elimination, with application to optical tweezers and atomic force microscope cantilevers. *Rev. Sci. Instrum.* **81**, 75103 (2009).
35. Han, L. I. N. *et al.* Calibration of tethered particle motion experiments. in *Mathematics of DNA Structure, Function and Interactions* 123–138 (Springer New York, 2009).
36. Dunlap, D. *et al.* Distinct contributions of MSL complex subunits to the transcriptional enhancement responsible for dosage compensation in *Drosophila*. *Nucleic Acids Res.* **40**, 11281–91 (2012).
37. Ritort, F. Single-molecule experiments in biological physics: methods and applications. *J. Phys. Condens. Matter* **18**, R531–R583 (2006).
38. Heller, I., Hoekstra, T. P., King, G. A., Peterman, E. J. G. & Wuite, G. J. L. Optical

- Tweezers Analysis of DNA – Protein Complexes. (2014).
39. Yang, G. *et al.* Solid-state synthesis and mechanical unfolding of polymers of T4 lysozyme. *Proc. Natl. Acad. Sci.* **97**, 139–144 (2000).
 40. van Loenhout, M. T. J., Kerssemakers, J. W. J., De Vlaminck, I. & Dekker, C. Non-Bias-Limited Tracking of Spherical Particles, Enabling Nanometer Resolution at Low Magnification. *Biophys. J.* **102**, 2362–2371 (2012).
 41. Gross, P., Farge, G., Peterman, E. J. G. & Wuite, G. J. L. Combining Optical Tweezers, Single-Molecule Fluorescence Microscopy, and Microfluidics for Studies of DNA–Protein Interactions. in *Methods in Enzymology* **475**, 427–453 (Elsevier Inc., 2010).
 42. King, L. V. On the Acoustic Radiation Pressure on Spheres. *Proc. R. Soc. A Math. Phys. Eng. Sci.* **147**, 212–240 (1934).
 43. Groschl, M. Ultrasonic Separation of Suspended Particles - Part I : Fundamentals. *Acustica* **84**, 432–447 (1998).
 44. Gor'kov L.P. On the forces acting on a small particle placed int an acoustic field in an ideal liquid. *Sov. Physics- Dokl.* **6**, 773–775 (1962).
 45. Krimholtz, R., Leedom, D. A. & Matthaei, G. L. New equivalent circuits for elementary piezoelectric transducers. *Electron. Lett.* **6**, 398 (1970).
 46. White, F. E. Fundamentals of Acoustics by Lawrence E. Kinsler, Austin R. Frey, Alan B. Coppers, and James V. Sanders. *J. Acoust. Soc. Am.* **72**, 1090 (1982).
 47. Bruus, H. Acoustofluidics 2: Perturbation theory and ultrasound resonance modes. *Lab Chip* **12**, 20 (2012).
 48. Brodie, G. W. J., Qiu, Y., Cochran, S., Spalding, G. C. & MacDonald, M. P. Optically transparent piezoelectric transducer for ultrasonic particle manipulation. *IEEE Trans. Ultrason. Ferroelectr. Freq. Control* **61**, 389–91 (2014).
 49. King, G. A. *et al.* Revealing the competition between peeled ssDNA, melting bubbles, and S-DNA during DNA overstretching using fluorescence microscopy. *Proc. Natl. Acad. Sci.* **110**, 3859–3864 (2013).
 50. Petersson, F., Nilsson, A., Holm, C., Jonsson, H. & Laurell, T. Continuous separation of lipid particles from erythrocytes by means of laminar flow and acoustic standing wave forces. *Lab Chip* **5**, 20 (2005).
 51. Evander, M. *et al.* Noninvasive acoustic cell trapping in a microfluidic perfusion system for online bioassays. *Anal. Chem.* **79**, 2984–2991 (2007).
 52. Mishra, P., Hill, M. & Glynn-Jones, P. Deformation of red blood cells using acoustic radiation forces. *Biomicrofluidics* **8**, 34109 (2014).
 53. Monson, C. F. *et al.* Antibody-Antigen Equilibria in a Field of Magnetic Forces: Design of Reagentless Biosensors. in *ECS Transactions* 79–91 (ECS, 2009). doi:10.1149/1.3118540
 54. ELLIS, R. W. & SOBANSKI, M. A. Diagnostic particle agglutination using ultrasound: a new technology to rejuvenate old microbiological methods. *J. Med. Microbiol.* **49**, 853–859 (2000).
 55. Sobanski, M. a *et al.* Ultrasound enhanced detection of individual meningococcal serogroups by latex immunoassay. *J. Clin. Pathol.* **55**, 37–40 (2002).
 56. Janssen, X. J. a, van IJzendoorn, L. J. & Prins, M. W. J. On-chip manipulation and detection of magnetic particles for functional biosensors. *Biosens. Bioelectron.* **23**, 833–838 (2008).

57. Brouwer, I. *et al.* Sliding sleeves of XRCC4–XLF bridge DNA and connect fragments of broken DNA. *Nat. Publ. Gr.* **535**, 566–569 (2016).
58. Yang, D., Ward, A., Halvorsen, K. & Wong, W. P. Multiplexed single-molecule force spectroscopy using a centrifuge. *Nat. Commun.* **7**, 11026 (2016).
59. Visser, E. W. A., van IJzendoorn, L. J. & Prins, M. W. J. Particle Motion Analysis Reveals Nanoscale Bond Characteristics and Enhances Dynamic Range for Biosensing. *ACS Nano* **10**, 3093–3101 (2016).
60. Broekmans, O. D., King, G. A., Stephens, G. J. & Wuite, G. J. L. DNA Twist Stability Changes with Magnesium(2+) Concentration. *Phys. Rev. Lett.* **116**, 258102 (2016).
61. Koonin, E. V., Senkevich, T. G. & Dolja, V. V. No Title. *Biol. Direct* **1**, 29 (2006).
62. Gelderblom, H. R. Structure and Classification of Viruses. in *Medical Microbiology* (ed. Baron, S.) (University of Texas Medical Branch at Galveston, 1996).
63. Yuen, K. *et al.* Clinical features and rapid viral diagnosis of human disease associated with avian influenza A H5N1 virus. *Lancet* **351**, 467–471 (1998).
64. WASSERHEIT, J. N. Epidemiological Synergy: Interrelationships between Human Immunodeficiency Virus Infection and Other Sexually Transmitted Diseases. *Sex. Transm. Dis.* **19**, (1992).
65. Mah, C., Byrne, B. J. & Flotte, T. R. Virus-Based Gene Delivery Systems. *Clin. Pharmacokinet.* **41**, 901–911 (2002).
66. Rohovie, M. J., Nagasawa, M. & Swartz, J. R. Virus-like particles: Next-generation nanoparticles for targeted therapeutic delivery. *Bioeng. Transl. Med.* **2**, 43–57 (2017).
67. Yang, N. An overview of viral and nonviral delivery systems for microRNA. *Int. J. Pharm. Investig.* **5**, 179 (2015).
68. Peer, D. *et al.* Nanocarriers as an emerging platform for cancer therapy. *Nat. Nanotechnol.* **2**, 751–760 (2007).
69. Ensign, L. M. *et al.* Mucus-Penetrating Nanoparticles for Vaginal Drug Delivery Protect Against Herpes Simplex Virus. *Sci. Transl. Med.* **4**, 138ra79-138ra79 (2012).
70. Zeng, Q. *et al.* Cucumber mosaic virus as drug delivery vehicle for doxorubicin. *Biomaterials* **34**, 4632–4642 (2013).
71. São-José, C., de Frutos, M., Raspaud, E., Santos, M. A. & Tavares, P. Pressure Built by DNA Packing Inside Virions: Enough to Drive DNA Ejection in Vitro, Largely Insufficient for Delivery into the Bacterial Cytoplasm. *J. Mol. Biol.* **374**, 346–355 (2007).
72. Rao, V. B. & Feiss, M. The Bacteriophage DNA Packaging Motor. *Annu. Rev. Genet.* **42**, 647–681 (2008).
73. Perlmutter, J. D., Qiao, C. & Hagan, M. F. Viral genome structures are optimal for capsid assembly. *Elife* **2013**, 1–21 (2013).
74. Perlmutter, J. D., Perkett, M. R. & Hagan, M. F. SI Pathways for virus assembly around nucleic acids. *J. Mol. Biol.* **426**, 3148–3165 (2014).
75. Mukherjee, S., Kler, S., Oppenheim, A. & Zlotnick, A. Uncatalyzed assembly of spherical particles from SV40 VP1 pentamers and linear dsDNA incorporates both low and high cooperativity elements. *Virology* **397**, 199–204 (2010).
76. Kler, S. *et al.* RNA encapsidation by SV40-derived nanoparticles follows a rapid two-state mechanism. *J. Am. Chem. Soc.* **134**, 8823–8830 (2012).

77. Kanesashi, S. N. *et al.* Simian virus 40 VP1 capsid protein forms polymorphic assemblies in vitro. *J. Gen. Virol.* **84**, 1899–1905 (2003).
78. Tsukamoto, H. *et al.* Evidence that SV40 VP1-DNA interactions contribute to the assembly of 40-nm spherical viral particles. *Genes to Cells* **12**, 1267–1279 (2007).
79. Hernandez-Garcia, A. *et al.* Design and self-assembly of simple coat proteins for artificial viruses. *Nat. Nanotechnol.* **9**, 698–702 (2014).
80. Hernandez-Garcia, A., Wertén, M. W. T., Stuart, M. C., De Wolf, F. A. & De Vries, R. Coating of single DNA molecules by genetically engineered protein diblock copolymers. *Small* **8**, 3491–3501 (2012).
81. Krejchi, M. T. *et al.* Chemical Sequence Control of β -Sheet Assembly in Macromolecular Crystals of Periodic Polypeptides Published by: American Association for the Advancement of Science Stable URL : <http://www.jstor.org/stable/2884827> JSTOR is a not-for-profit service that he. **265**, 1427–1432 (2017).
82. Beun, L. H., Beaudoux, X. J., Kleijn, J. M., De Wolf, F. A. & Cohen Stuart, M. A. Self-assembly of silk-collagen-like triblock copolymers resembles a supramolecular living polymerization. *ACS Nano* **6**, 133–140 (2012).
83. Mukherjee, S. *et al.* High cooperativity of the SV40 major capsid protein VP1 in virus assembly. *PLoS One* **2**, (2007).
84. Pace, C. N., Vajdos, F., Fee, L., Grimsley, G. & Gray, T. How To Measure and Predict the Molar Absorption-Coefficient of a Protein. *Protein Sci.* **4**, 2411–2423 (1995).
85. Wang, M. D., Yin, H., Landick, R., Gelles, J. & Block, S. M. Stretching DNA with optical tweezers. *Biophys. J.* **72**, 1335–1346 (1997).
86. Stehle, T., Gamblin, S. J., Yan, Y. & Harrison, S. C. The structure of simian virus 40 refined at 3.1 Å resolution. *Structure* **4**, 165–182 (1996).
87. Ishizu, K. I. *et al.* Roles of disulfide linkage and calcium ion-mediated interactions in assembly and disassembly of virus-like particles composed of simian virus 40 VP1 capsid protein. *J. Virol.* **75**, 61–72 (2001).
88. Yang, H. Change-Point Localization and Wavelet Spectral Analysis of Single-Molecule Time Series. in *Single Molecule Biophysics: Experiment and Theory* **146**, 217–243 (2011).
89. Kler, S., Wang, J. C. Y., Dhasan, M., Oppenheim, A. & Zlotnick, A. Scaffold properties are a key determinant of the size and shape of self-assembled virus-derived particles. *ACS Chem. Biol.* **8**, 2753–2761 (2013).
90. Kimchi-Sarfaty, C., Arora, M., Sandalon, Z., Oppenheim, A. & Gottesman, M. M. High cloning capacity of in vitro packaged SV40 vectors with no SV40 virus sequences. *Hum. Gene Ther.* **14**, 167–177 (2003).
91. Kimchi-Sarfaty, C., Ben-Nun-Shaul, O., Rund, D., Oppenheim, A. & Gottesman, M. M. In vitro-packaged SV40 pseudovirions as highly efficient vectors for gene transfer. *Hum. Gene Ther.* **13**, 299–310 (2002).
92. Takahashi, R. u. *et al.* Presentation of functional foreign peptides on the surface of SV40 virus-like particles. *J. Biotechnol.* **135**, 385–392 (2008).
93. Jaqaman, K. *et al.* Robust single-particle tracking in live-cell time-lapse sequences. *Nat. Methods* **5**, 695–702 (2008).
94. Ohyama, T. *DNA Conformation and Transcription.* *BioScience* (Springer US, 2005). doi:10.1007/0-387-29148-2

95. Nudler, E. RNA polymerase active center: the molecular engine of transcription. *Annu. Rev. Biochem.* **78**, 335–61 (2009).
96. Okazaki, K.-I. & Takada, S. Dynamic energy landscape view of coupled binding and protein conformational change: induced-fit versus population-shift mechanisms. *Proc. Natl. Acad. Sci. U. S. A.* **105**, 11182–11187 (2008).
97. Rosenbaum, D. M., Rasmussen, S. G. F. & Kobilka, B. K. The structure and function of G-protein-coupled receptors. *Nature* **459**, 356–363 (2014).
98. Tama, F. & Sanejouand, Y.-H. Conformational change of proteins arising from normal mode calculations. *Protein Eng. Des. Sel.* **14**, 1–6 (2001).
99. Dill, K. a & MacCallum, J. L. The protein-folding problem, 50 years on. *Science* **338**, 1042–6 (2012).
100. Levinthal, C. How to fold graciously. *Mössbauer Spectrosc. Biol. Syst. Proc.* **24**, 22–24 (1969).
101. Sivertsson, E. M. & Itzhaki, L. S. Protein folding: When ribosomes pick the structure. *Nat. Chem.* **6**, 378–9 (2014).
102. Young, J. C., Agashe, V. R., Siegers, K. & Hartl, F. U. Pathways of chaperone-mediated protein folding in the cytosol. *Nat. Rev. Mol. Cell Biol.* **5**, 781–791 (2004).
103. Clarke, A. R. Molecular chaperones in protein folding and translocation. *Curr. Opin. Struct. Biol.* **6**, 43–50 (1996).
104. NUKINA, N. & IHARA, Y. Proteolytic Fragments of Alzheimer's Paired Helical Filaments1. *J. Biochem.* **98**, 1715–1718 (1985).
105. Chiti, F. & Dobson, C. M. Protein Misfolding, Functional Amyloid, and Human Disease. *Annu. Rev. Biochem.* **75**, 333–366 (2006).
106. Cooper, S. *et al.* Predicting protein structures with a multiplayer online game. *Nature* **466**, 756–760 (2010).
107. Pirchi, M. *et al.* Single-molecule fluorescence spectroscopy maps the folding landscape of a large protein. *Nat. Commun.* **2**, 493 (2011).
108. Ha, T. *et al.* Single-molecule fluorescence spectroscopy of enzyme conformational dynamics and cleavage mechanism. *Proc. Natl. Acad. Sci.* **96**, 893–898 (1999).
109. Kuwajima, K., Yamaya, H., Miwa, S., Sugai, S. & Nagamura, T. Rapid formation of secondary structure framework in protein folding studied by stopped-flow circular dichroism. *FEBS Lett.* **221**, 115–118 (1987).
110. Chan, C. K. *et al.* Submillisecond protein folding kinetics studied by ultrarapid mixing. *Proc. Natl. Acad. Sci. U. S. A.* **94**, 1779–1784 (1997).
111. Zlatanova, J., Lindsay, S. M. & Leuba, S. H. Single molecule force spectroscopy in biology using the atomic force microscope. *Prog. Biophys. Mol. Biol.* **74**, 37–61 (2000).
112. Mossa, A., Hugué, J. M. & Ritort, F. Investigating the thermodynamics of small biosystems with optical tweezers. *Phys. E Low-Dimensional Syst. Nanostructures* **42**, 666–671 (2010).
113. Bell, G. Models for the specific adhesion of cells to cells. *Science (80-.)*. **200**, 618–627 (1978).
114. Ritort, F., Bustamante, C. & Tinoco, I. A two-state kinetic model for the unfolding of single molecules by mechanical force. *Proc. Natl. Acad. Sci. U. S. A.* **99**, 13544–13548 (2002).

115. De Vlaminck, I. *et al.* Highly parallel magnetic tweezers by targeted DNA tethering. *Nano Lett.* **11**, 5489–93 (2011).
116. Forns, N. *et al.* Improving signal/noise resolution in single-molecule experiments using molecular constructs with short handles. *Biophys. J.* **100**, 1765–1774 (2011).
117. Zhou, R., Berne, B. J. & Germain, R. The free energy landscape for beta hairpin folding in explicit water. *Proc. Natl. Acad. Sci. USA* **98**, 14931–6 (2001).
118. Tan, Z.-J. & Chen, S.-J. Salt dependence of nucleic acid hairpin stability. *Biophys. J.* **95**, 738–752 (2008).
119. Alemany, A. & Ritort, F. Force-Dependent Folding and Unfolding Kinetics in DNA Hairpins Reveals Transition-State Displacements along a Single Pathway. *J. Phys. Chem. Lett.* **8**, 895–900 (2017).
120. Evans, E. & Ritchie, K. Dynamic strength of molecular adhesion bonds. *Biophys. J.* **72**, 1541–55 (1997).
121. Bizarro, C. V., Alemany, A. & Ritort, F. Non-specific binding of Na⁺ and Mg²⁺ to RNA determined by force spectroscopy methods. *Nucleic Acids Res.* **40**, 6922–6935 (2012).
122. Dudko, O. K., Hummer, G. & Szabo, A. Theory, analysis, and interpretation of single-molecule force spectroscopy experiments. *Proc. Natl. Acad. Sci.* **105**, 15755–15760 (2008).
123. Manosas, M., Collin, D. & Ritort, F. Force-dependent fragility in RNA hairpins. *Phys. Rev. Lett.* **96**, 5–8 (2006).
124. SantaLucia, J. A unified view of polymer, dumbbell, and oligonucleotide DNA nearest-neighbor thermodynamics. *Proc. Natl. Acad. Sci. U. S. A.* **95**, 1460–5 (1998).
125. Huguet i Casades, J. M. Statistical and thermodynamic properties of DNA unzipping experiments with optical tweezers. (2010).
126. Bustamante, C., Marko, J. F., Siggia, E. D. & Smith, S. Entropic Elasticity of X-Phage DNA Explicit and Implicit Learning and Maps of Cortical Motor Output. *Science (80-.)*. **265**, 1599–1600 (1994).
127. Alemany, A. Dynamic force spectroscopy and folding kinetics in molecular systems. *Thesis* (2014).
128. Hänggi, P., Talkner, P. & Borkovec, M. Reaction-rate theory: fifty years after Kramers. *Rev. Mod. Phys.* **62**, 251–341 (1990).
129. Bustamante, C., Chemla, Y. R., Forde, N. R. & Izhaky, D. Mechanical Processes in Biochemistry. *Annu. Rev. Biochem.* **73**, 705–748 (2004).
130. Mossa, A., Manosas, M., Forns, N., Huguet, J. M. & Ritort, F. Dynamic force spectroscopy of DNA hairpins: I. Force kinetics and free energy landscapes. *J. Stat. Mech. Theory Exp.* **2009**, P02060 (2009).
131. Dulin, D. *et al.* High Spatiotemporal-Resolution Magnetic Tweezers: Calibration and Applications for DNA Dynamics. *Biophys. J.* **109**, 2113–2125 (2015).
132. Schmied, J. J. *et al.* DNA origami nanopillars as standards for three-dimensional superresolution microscopy. *Nano Lett.* **13**, 781–785 (2013).
133. Pfitzner, E. *et al.* Rigid DNA beams for high-resolution single-molecule mechanics. *Angew. Chemie - Int. Ed.* **52**, 7766–7771 (2013).
134. Ley, K., Laudanna, C., Cybulsky, M. I. & Nourshargh, S. Getting to the site of inflammation: the leukocyte adhesion cascade updated. *Nat. Rev. Immunol.* **7**,

- 678–689 (2007).
135. Li, F., Redick, S. D., Erickson, H. P. & Moy, V. T. Force measurements of the alpha5beta1 integrin-fibronectin interaction. *Biophys. J.* **84**, 1252–1262 (2003).
 136. Kim, S.-H., Chegal, W., Doh, J., Cho, H. M. & Moon, D. W. Study of Cell-Matrix Adhesion Dynamics Using Surface Plasmon Resonance Imaging Ellipsometry. *Biophys. J.* **100**, 1819–1828 (2011).
 137. Lu, H. *et al.* Microfluidic shear devices for quantitative analysis of cell adhesion. *Anal. Chem.* **76**, 5257–5264 (2004).
 138. Boettiger, D. Quantitative Measurements of Integrin-Mediated Adhesion to Extracellular Matrix. *Methods Enzymol.* **426**, 1–25 (2007).
 139. García, A. J., Huber, F. & Boettiger, D. Force required to break alpha5beta1 integrin-fibronectin bonds in intact adherent cells is sensitive to integrin activation state. *J. Biol. Chem.* **273**, 10988–10993 (1998).
 140. Reyes, C. D. & García, A. J. A centrifugation cell adhesion assay for high-throughput screening of biomaterial surfaces. *J. Biomed. Mater. Res. A* **67**, 328–33 (2003).
 141. Marx, V. Biophysics: using sound to move cells. *Nat. Methods* **12**, 41–44 (2014).
 142. Laurell, T., Petersson, F. & Nilsson, A. Chip integrated strategies for acoustic separation and manipulation of cells and particles. *Chem. Soc. Rev.* **36**, 492–506 (2007).
 143. Petersson, F., Åberg, L., Swärd-Nilsson, A. M. & Laurell, T. Free flow acoustophoresis: Microfluidic-based mode of particle and cell separation. *Anal. Chem.* **79**, 5117–5123 (2007).
 144. Rose, T. *et al.* Interleukin-7 compartmentalizes its receptor signaling complex to initiate CD4 T lymphocyte response. *J. Biol. Chem.* **285**, 14898–908 (2010).
 145. Tamarit, B. *et al.* Membrane microdomains and cytoskeleton organization shape and regulate the IL-7 receptor signalosome in human CD4 T-cells. *J. Biol. Chem.* **288**, 8691–8701 (2013).
 146. Butcher, E. C. Leukocyte-endothelial cell recognition: Three (or more) steps to specificity and diversity. *Cell* **67**, 1033–1036 (1991).
 147. Schnoor, M., Alcaide, P., Voisin, M. B. & Van Buul, J. D. Crossing the Vascular Wall: Common and Unique Mechanisms Exploited by Different Leukocyte Subsets during Extravasation. *Mediators Inflamm.* **2015**, (2015).
 148. Springer, T. A. Traffic signals for lymphocyte recirculation and leukocyte emigration: The multistep paradigm. *Cell* **76**, 301–314 (1994).
 149. Spengler, J. F., Coakley, W. T. & Christensen, K. T. Microstreaming effects on particle concentration in an ultrasonic standing wave. *AIChE J.* **49**, 2773–2782 (2003).
 150. Bernhagen, D., De Laporte, L. & Timmerman, P. High-Affinity RGD-Knottin Peptide as a New Tool for Rapid Evaluation of the Binding Strength of Unlabeled RGD-Peptides to $\alpha\beta3$, $\alpha\beta5$, and $\alpha5\beta1$ Integrin Receptors. *Anal. Chem.* **89**, 5991–5997 (2017).
 151. Lenshof, A., Evander, M., Laurell, T. & Nilsson, J. Acoustofluidics 5: Building microfluidic acoustic resonators. *Lab Chip* **12**, 684 (2012).
 152. Ophir, J. & Parker, K. J. Contrast agents in diagnostic ultrasound. *Ultrasound Med. Biol.* **15**, 319–333 (1989).

153. Kokhuis, T. J. A. *et al.* Secondary Bjerknes Forces Deform Targeted Microbubbles. *Ultrasound Med. Biol.* **39**, 490–506 (2013).
154. Kothapalli, S. V. V. N., Wiklund, M., Janerot-Sjoberg, B., Paradossi, G. & Grishenkov, D. Investigation of polymer-shelled microbubble motions in acoustophoresis. *Ultrasonics* **70**, 275–283 (2016).
155. Augustsson, P. *et al.* Measuring the Acoustophoretic Contrast Factor of Living Cells in Microchannels. *Cell* 1337–1339 (2010).
156. Mathieu, P. S. & Lobo, E. G. Cytoskeletal and Focal Adhesion Influences on Mesenchymal Stem Cell Shape, Mechanical Properties, and Differentiation Down Osteogenic, Adipogenic, and Chondrogenic Pathways. *Tissue Eng. Part B Rev.* **18**, 436–444 (2012).
157. Discher, D. E. Tissue Cells Feel and Respond to the Stiffness of Their Substrate. *Science (80-.)*. **310**, 1139–1143 (2005).
158. Cross, S. E., Jin, Y.-S., Rao, J. & Gimzewski, J. K. Nanomechanical analysis of cells from cancer patients. *Nat. Nanotechnol.* **2**, 780–783 (2007).
159. Maciaszek, J. L., Andemariam, B. & Lykotrafitis, G. Microelasticity of red blood cells in sickle cell disease. *J. Strain Anal. Eng. Des.* **46**, 368–379 (2011).
160. Suresh, S. *et al.* Reprint of: Connections between single-cell biomechanics and human disease states: gastrointestinal cancer and malaria. *Acta Biomater.* **23**, S3–S15 (2015).
161. Thomas, G., Burnham, N. A., Camesano, T. A. & Wen, Q. Measuring the Mechanical Properties of Living Cells Using Atomic Force Microscopy. *J. Vis. Exp.* 1–8 (2013). doi:10.3791/50497
162. Guevorkian, K., Manzi, J., Pontani, L. L., Brochard-Wyart, F. & Sykes, C. Mechanics of Biomimetic Liposomes Encapsulating an Actin Shell. *Biophys. J.* **109**, 2471–2479 (2015).
163. Koch, M. *et al.* *Plasmodium falciparum* erythrocyte-binding antigen 175 triggers a biophysical change in the red blood cell that facilitates invasion. *Proc. Natl. Acad. Sci.* **114**, 4225–4230 (2017).
164. Wei, J. F., Sun, K., Xu, S. G., Xie, H. Y. & Zheng, S. Sen. Inhibition of PMA-induced endothelial cell activation and adhesion by over-expression of domain negative I κ B α protein. *World J. Gastroenterol.* **11**, 3080–3084 (2005).
165. Moser, M., Legate, K. R., Zent, R. & Fassler, R. The Tail of Integrins, Talin, and Kindlins. *Science (80-.)*. **324**, 895–899 (2009).
166. Seventer, G. A. Van, Shimizu, Y. & Shaw, J. H. and S. The LFA-1 ligand ICAM-1 provides an important costimulatory signal for T cell receptor-mediated activation of resting T cells. *J. Immunology* **144**, 4579–4589 (2017).

Publications list

1. Douwe Kamsma*, Gerrit Sitter* Gregor Thalhammer, Monika Ritsch-Marte, Erwin J.G. Peterman† & Gijs J.L. Wuite†; *Acoustic force spectroscopy*; *Nature Methods*, 12, 47–50 (2014). (**Chapter 2**)
2. Douwe Kamsma, Ramon Creyghton, Gerrit Sitters, Gijs J.L. Wuite† & Erwin J.G. Peterman†; *Acoustic force spectroscopy 2.0: Tuning the music*; *Methods* 102, 26–33 (2016). (**Chapter 3**)
3. Douwe Kamsma & Gijs J.L. Wuite; *Single Molecule Analysis. Methods in Molecular Biology*, Chapter 18, 1665, 341–351 (2017). (**Chapter 4**)
4. Douwe Kamsma*, Pascal Bochet*, Felix Oswald, Nander Ablas, Sophie Goyard, Gijs J. L. Wuite†, Erwin J. G. Peterman† & Thierry Rose†; *Single-Cell Acoustic Force Spectroscopy (scAFS): Resolving kinetics and strength of T-cell adhesion to fibronectin; under review at Cell Reports* (**Chapter 7**)
5. Margherita Marchetti, Douwe Kamsma, Renko de Vries, Paul van der Schoot, Wouter H. Roos & Gijs J.L. Wuite; *Real-time investigation of the assembly dynamics of an artificial virus-like particle; manuscript in preparation* (**Chapter 5**)
6. Mariska G.M. van Rosmalen, Douwe Kamsma, Andreas S. Biebricher, Chenlei Li, Adam Zlotnick, Wouter H. Roos and Gijs J.L. Wuite; *Real-time assembly of SV40 VP1 capsids onto DNA studied using Optical Tweezers and Acoustic Force Spectroscopy; manuscript in preparation* (**Chapter 5**)
7. Raya Sorkin*, Giulia Bergamaschi*, Douwe Kamsma, Guy Brand, Elya Dekel, Yifat Ofir-Birin, Neta, Regev-Rudzki, Wouter Roos and Gijs J.L. Wuite; *Probing cellular mechanics with Acoustic Force Spectroscopy; manuscript submitted in Molecular Biology of the Cell* (**Chapter 9**)

*, † These authors contributed equally.

Acknowledgements

A PhD can be very personal and lonely, however, I have not experienced it in that way thanks to all the people surrounding me, inside and outside the university. The COSY group has become a second home to me, I have seen many people come and go, but I have always enjoyed it and above all it has given me the opportunity to make many amazing friends. It is with pain in my heart that I have to leave this place. In this last part of my thesis I want to express my gratitude to everybody who has helped me directly and indirectly to produce this book.

First of all, I would like to express my gratitude to my supervisors **Erwin** and **Gijs**, the super team, that gave me the opportunity to continue with my AFS machine (or acoustic pushing by that time), without having direct funding for this project. After four different temporal contracts, also Gijs got lost and almost extended my contract for one year extra. To **Erwin**, thank you for always being critical, patient and extremely precise with everything you do. Especially in the writing process, I have learned a lot from you. After your comments, on any kind of text produced by me, I was always confused if the font color was already red or not. I remember telling you this one time, and you happily replied to me that it is possible to set the track changes to a different color. To **Gijs**, I want to thank you for always being positive and enthusiastic about my science. After each of our meetings, I was always uplifted and excited again about my research. I really admire your creativity and the ability to see the value in any kind of data and make a story out of it. It has really increased the value of the work in this thesis. The synergy between the skillsets of you and that of Erwin has helped me a lot during the course of my PhD!

Gerrit, you have been my supervisor during my master project, and together, we have started the AFS project. Not only was it a great success from the start, it also inspired me to stay in Science and it really gave me a kickstart into my PhD. You are still one of the smartest people I know and I have learned a great

deal from you, thank you for all of that!

Thank you **Daisuke**, **Leo**, **Davide**, **Anders** and **Claire** for the time you have spent on my thesis as a member of the reading committee and/or opposition.

Raya, you are one of the most driven persons and also one of the most emotionally attached to science I have ever met. I remember when we were measuring together and during the day your thoughts could jump from “*we are going to publish multiple Nature articles together*” to “*everything is shit, not interesting and it is better if we stop it now*”. These two extremes were oscillating during the day. Although we had our ups and downs, I am very happy that we worked together. Maybe no Nature articles yet, but we will see what the future will bring. I wish you all the best with your scientific career, I am sure you will succeed!!!

Megghi and **Mariska**, the little virus girls, your personalities are so different, and yet you both end up in the same chapter of my thesis. Mariska, I appreciate your calm, peaceful and very precise way of working. It is not that you do not care, but it seems that any kind of setback in your working life is not affecting you at all. I think that is an amazing skill and many people could learn a lot from that. It will not be too long before I also get your book and hopefully we get that article published as well! **Meg**, you are crazy, no joke!, and especially in combination with your Irish friend, you guys are out of control. I mean this of course in the best possible way, we had many odd moments that I should better not mention here. I also enjoyed our scientific project together, experiencing also a very serious side of you. Good luck with the last year of your PhD.

Many thanks also to my students for all the work during their internships. **Ramon**, I explained you in the beginning of your project what the problem was, and after that you just worked on it for two months and now your work is part of a publication, great job! If you do your PhD with the same independent attitude, it will definitely be a success. **Luuk**, unfortunately science can be quite a struggle. Don't let it get you down, because building a TIRF system and doing some useful measurements within a couple of weeks is almost impossible. **Nander**, I think you did a great job during your internship and hopefully there will be article out soon with your name on it. Besides that, it has also let you to your current job and soon we will be colleagues again. **Tudor**, it was great to have my first encounter with somebody from Moldova. I know a thesis can appear as big frightening mountain, but I am certain you will reach the top with a lot of joy and pride.

Thanks also to all my collaborators. **Monika** and **Gregor**, the AFS idea has found its existence in your lab even before I was in the picture, thank you for all the help we got from your side. **Thierry**, thank you for all the enthusiasm you have brought together with all your cells in the night bus from Paris to the VU, I hope we publish our article soon! **Haroon, Richard, Jenneke** and **Astrid** thank you for teaching me so much about cells, unfortunately they were not always willing to listen to the AFS. **Hanke** and **Michel**, we just started up our project let's see what you guys can do with it.

Fabio and **Felix** thanks in advance for taking up the burden of being a paranymph and standing beside me on the stage. I want to thank you both for being great friends, when needed I know I can always count on you! **Felix**, the helper, as labelled by your new employer, but already clear to everybody for a long time. Your intrinsic enthusiasm, openness to new thing and helpfulness have led to many interesting activities, such as bathtub chess, basement saving against the flood, new year's dives and many Lamesons. I hope that even though the boat is gone there will still be many parties in the future. **Fabio**, we started together in the Master, scavenger hunts in Uilenstede, boat rides and cooking 'real' Bolognese. I am happy that this continued in the PhD with beach volleyball, fishing catfish at your grandmother's farm and the most amazing road trip in the States, where you taught me how to make campfires and have the best weakyleaks moments. Many great memories to cherish, let's make sure we keep on making new ones!

I want to thank all the other people that made my PhD into a great experience during the years. **Karsta**, we started our Master together and I really enjoyed all beach volleyball, cappuccini break, boat rides and all the other activities we have done. I was really sad when you decided to move and do your PhD in France, however, that also meant a super nice holiday opportunity, where (if you are very lucky) you can see flamingos. **Jules**, good food, good wine and ... some friends, luckily we (the friends) are still on the list. Hope to see you often in the future as well. **Den**, as I mentioned before, you are crazy, only because I learned from you that this is the greatest compliment you can get. Besides all the laughing, I also want to thank you for reading and commenting on parts of this thesis!

To all the old COSY group members, thank you for making me feel welcome in your club. I felt it from the beginning, partly due to all the social activities organized in the group like, hard liquor parties, beach volleyball matches, murder mystery games and crazy Odoorn weekends. **Tjalle, Andrea, Daan** and

Bram (Prevo), I came in your very male dominated U-030 room at the start of the PhD, although you already formed some strong friendships and most of you were at the end of the journey, I still felt very welcome here. Of course, this was also thanks to all the non-office mates, **Marian, Aravinda, Els, Onno**, the programming guru, thank you for helping me with my newbie programming problems and informing me about the most diverse facts during the coffee breaks. **Niels**, thanks for all the great times at the beach volleyball court. **Ineke**, I love your unrestrained options, but also your kindness and the fact that you are always there to help others.

Then, there are the constant forces in our group. **Andreas** the chemist master, I always enjoyed the deep and elaborated discussion if one of my protocols was not working anymore. **Seyda**, the DNA master, always willing to help others and most of the time have the correct solution ready. **Iddo** and **Wouter**, the newly fabricated PI's, it is great to see your development and I wish you all the best with your careers. **Graeme**, at work a highly focused person, however in your free time I experienced that you transform in a very social and active person. **Sandrine**, my DNA maker, thank for the many pKYB1 sample you made for me and all the great pics during the group activities, maybe you can shoot some as well during my defense?

Then there is the new COSY generation of the group **Anna** and **Julia**, our own lab safety inspectors. Besides being serious about your work, I can often hear you laugh from the other side of the office, luckily I can often participate in the fun. **Jaap**, the peanut butter with hagelslag guy, I'm happy you were there to fight against the female take over, I'm sorry that I have to leave you behind now. **Ning** and **Vandana**, I really enjoyed the presence of you both and I hope I receive your books soon as well. Mother **Marjam**, don't put yourself to the background, you have a lot of interesting stuff to say as well! Hopefully your sample will be ready soon (finally, after 2 maybe 3 years), so you can start your own AFS adventure, good luck! **Lungfu**, in your first month you were already allowed to dress up like a power ranger and I haven't seen a PhD student with a happier face. **Dian**, finally you found the house and the boyfriend is coming along as well, I hope this gives you some rest. Good luck to you all with your PhD's and postdoc's, it is with pain in my heart that I have to leave this amazing group.

Kiki, my new AFS apprentice. It is an honor transferring all my AFS knowledge to such a smart and fast learning person. If you keep up this pace, I am sure you will have a great PhD. May the acoustic force be with you!

Jordi, I don't know if you belong to the new or the old generation of our lab, but you're one of the most social persons I have met and I am very happy to become your colleague again.

Thanks also to the lab's long-term visitors, you all contributed to the nice atmosphere in the in group! **Tianglong, Yan, Hongshan** and many more, like **Kathy**, although not working here anymore, you made a more permanent connection to our lab. The Bachelor and Master students **Ernst, Agata, Joost, Joey, Stella, Jasmijn, Rouquaya, Myrthe** and many others. **Giulia**, I have never seen such a driven and entrepreneurial master student, good luck finishing up and then with the PhD!

Thanks also to all the non COSY group member **Boy, Dirk, Max, Frank, Jelmer, Jianna, Joshua, Johannes, Judith, Kari, Leron, Mathi, Mattijs** and **Mirjam, Oleg**, for all the numerous coffee room break. **Bram** (Mooij), fixing computer, bikes or borrowing a drill, if you can help someone you always do. **Judith**, it was a very brave and strong decision not to finish the PhD, but it was definitely the best for you. I wish you guys all the best and thanks again for all the good times!

Marja, Régine en **Sandrijn**, Thank you for all the administrative work behind the scenes. Many thank as well as to **Pierre, Tim, Pieter**, and all the other people from the mechanical and the electrical workshop.

Luca and **Sev**, although you were not in my research group, I feel that you both are part of my 4 years journey. Both of you have an inexhaustible source of energy that always bring me in a good mood! Thank you guys for the many dinner, parties and beach volleyball days. Of course **Michael**, my partner in crime at the beach volleyball court, although since you are at TNO it is a bit harder to show up, I hope we can fight for the SVU title once more this year.

Lukas, Guido and **Chris**, my high school friends. I am very grateful we kept our strong bond over the years! Together with all extra friends that come with this group, **Dieter, Christopher, Hessel, Kumyl, Bram, Liza, Frederiek, Sitta, Özge, Esmeralda** and **Solange**, thank you all for the many distractions you guys have given me from my PhD!

LUMICKS, I am very grateful that this company came into existence, because it was very rewarding for me to see that the research I did was directly implemented in a product. Also, developments within LUMICKS could directly be used by me, resulting in a nice synergy. After a little mating dance we will

now be integrated as one. I, for sure, am very excited to start the new adventure with a team of very smart and driven people!

Mams and Paps, you produced three sons with very different professions: an artist (**Jaap**), a business man (**Bas**) and scientist (me). Even though it is sometimes hard to understand each other's world, everybody always tried and helped each other. Thanks for the support you all guys gave me during the last 4 years, but also for all the years before that!!!

Fede, you are the greatest gift that the PhD has given to me. Although we have met each other in the least romantic place I can imagine: the dark and wet basement of the VU, we already made it to the top of Amsterdam. My personal editor, besides being an amazing person in many aspects, you were also an enormous help to me in writing this thesis. As a dyslectic person I always feared the moment of having to write a whole book at the end of the PhD, but the fact that I could always count on you for proofreading any of my chapters has made it so much easier. Thank you for that and all the other support during my PhD! I hope I can return the favor in the future. I love you!