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Nota di contenuto	1 introduction 3 -- references 5 -- 2 intermediate filaments - from proteins to networks 9 -- 2.1 Structure and assembly of intermediate filament proteins 10 -- 2.2 Mechanical properties of single intermediate filaments 12 -- 2.2.1 Persistence length 12 -- 2.2.2 Stretching response . 13 -- 2.3 Networks of reconstituted intermediate filaments . 15 -- 2.4 Intermediate filament networks in cells . 16 -- 2.4.1 Structure and function of intermediate filament networks in cells 16 -- 2.4.2 Intermediate filament networks and cell mechanics 16 -- 2.4.3 Keratin networks in cells under load . 17 -- references 17 -- 3 biopolymer mechanics - theoretical and experimental principles 29 -- 3.1 Optical tweezers . 29 -- 3.1.1 Particle trapping 30 -- 3.1.2 Force detection . 31 -- 3.2 Microrheology 34 -- 3.2.1 Rheology of viscoelastic materials 34 -- 3.2.2 Passive microrheology: microparticle tracking . 34 -- 3.2.3 Active microrheology: optical trapping . 36 -- 3.3 Polymer mechanics . 38 -- 3.3.1 Entropic stretching of worm-like chains . 38 -- 3.3.2 Worm-like bundles . 39 -- 3.3.3 Networks of semiflexible polymers . 39 -- 3.4 Molecular reactions . 43 -- 3.4.1 Step-growth polymerization . 43 -- 3.4.2 Molecular reaction kinetics - two state models . 43 -- references 44 -- 4 materials and methods 51 -- 4.1 Vimentin preparation 51 -- 4.2 Maleimide functionalization of polystyrene beads . 52 -- 4.3 Stretching single filaments by optical trapping . 53 -- 4.4 Analysis of single filament mechanics 54 -- 4.5 Force-strain Monte-Carlo simulations 56 -- 4.6 Optical trap

measurements of individual filament-filament interactions . 56 -- 4.7 Analysis of the interaction data 58 -- 4.8 Microrheology of reconstituted vimentin networks . 60 -- 4.9 Analysis of microrheology experiments . 61 -- 4.10 Imaging filament networks 63 -- 4.11 Imaging single filaments 63 -- 4.12 Analysis of filament lengths 64 -- 4.13 Finite element simulation of the microfluidic flowcell . 64 -- 4.14 Stretching MDCK II cells on elastic substrates . 65 -- 4.15 Analysis of images of stretched cells . 68 -- references 70 -- 5 tuning intermediate filament mechanics by variation of -- ph and ion charges 75 -- 5.1 Introduction . 76 -- 5.2 Results and discussion . 77 -- 5.2.1 Cations stiffen single vimentin IFs 77 -- 5.2.2 Stretching vimentin filament bundles 81 -- 5.2.3 IF mechanics adapt to pH changes 82 -- 5.2.4 IF stiffening saturates at low pH . 83 -- 5.2.5 Variations in the free energy landscapes influence filament mechanics 85 -- 5.3 Conclusions . 90 -- references 91 -- 6 multiscale mechanics and temporal evolution of vimentin -- intermediate filament networks 97 -- 6.1 Introduction . 98 -- 6.2 Results and discussion . 98 -- 6.2.1 Vimentin filament networks mature and stiffen on time scales of days 98 -- 6.2.2 The filament length depends on elongation and lateral association 100 -- 6.2.3 Electrostatic and hydrophobic interactions lead to mechanically distinct networks 101 -- 6.2.4 Maturation of networks is concentration dependent 104 -- 6.2.5 Surface effects modify network structures . 105 -- 6.2.6 Single filament mechanics are unaffected by detergents or divalent ions . 107 -- 6.2.7 Electrostatics increase single filament-filament interactions 108 -- 6.2.8 Interactions are independent of binding-site encounter rate 112 -- 6.2.9 A two-state model accurately describes network mechanics 112 -- 6.3 Conclusions . 113 -- 6.4 Outlook 115 -- 6.4.1 Entropic and elastic stretching of single vimentin filaments 115 -- 6.4.2 Single interactions of pre-strained filaments 117 -- references 119 -- 7 response of actin and keratin structures to isotropic cell stretching 125 -- 7.1 Introduction . 125 -- 7.2 Results and Discussion . 126 -- 7.2.1 Equibiaxial stretching of PDMS devices . 126 -- 7.2.2 The cell area increases during isotropic stretching . 128 -- 7.2.3 Actin stress fibers disassemble at increasing cell extension 129 -- 7.2.4 The keratin structure adapts to increasing strains . 131 -- 7.3 Conclusion 133 -- references 133 -- 8 discussion and conclusion 137 -- references 140 -- appendix 145 -- a supporting information: tuning intermediate filament mechanics by variation of ph and ion charges 145 -- a.1 Flow simulations 145 -- a.2 Single force-strain curves . 147 -- b supporting information: multiscale mechanics and temporal evolution of vimentin intermediate filament networks 149 -- b.1 Additional information for elongation measurements . 149 -- b.2 Data analysis of microrheology measurements . 152 -- b.3 Modeling single interactions 161 -- c supporting information: response of actin and keratin structures to isotropic cell stretching 167 -- references 169 -- Acknowledgments 172 -- List of acronyms 174 -- Publications 176.

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## Sommario/riassunto

The mechanical properties of cells are largely determined by the cytoskeleton. The cytoskeleton is an intricate and complex structure formed by protein filaments, motor proteins, and crosslinkers. The three main types of protein filaments are microtubules, actin filaments, and intermediate filaments ( IFs ). Whereas the proteins that form microtubules and actin filaments are exceptionally conserved throughout cell types and organisms, the family of IFs is diverse. For example, the IF protein vimentin is expressed in relatively motile fibroblasts, and keratin IFs are found in epithelial cells. This variety of IF proteins might therefore be linked to the various mechanical properties of different cell types. In the scope of this thesis, I combine

studies of IF mechanics on different time scales and in systems of increasing complexity, from single filaments to networks in cells. This multiscale approach allows for the simplification necessary to interpret observations while adding increasing physiological context in subsequent experiments. We especially focus on the tunability of the IF mechanics by environmental cues in these increasingly complex systems. In a series of experiments, including single filament elongation studies, single filament stretching measurements with optical tweezers, filament-filament interaction measurements with four optical tweezers, microrheology, and isotropic cell stretching, we characterize how electrostatic (pH and ion concentration) and hydrophobic interactions (detergent) provide various mechanisms by which the mechanics of the IF cytoskeleton can be tuned. These studies reveal how small changes, such as charge shifts, influence IF mechanics on multiple scales. In combination with simulations, we determine the mechanisms by which charge shifts alter single vimentin filament mechanics and we extract energy landscapes for interactions between single filaments. Such insights will provide a deeper understanding of the mechanisms by which cells can maintain their integrity and adapt to the mechanical requirements set by their environment.

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