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| 1. Record Nr. | UNINA9910647245003321 |
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| Titolo | Intermediate filament mechanics across scales : from single filaments to single interactions and networks in cells // Anna Veronika Schepers |
| Pubbl/distr/stampa | Gottingen : , : Universitätsverlag Gottingen, , [2022] ©2022 |
| Descrizione fisica | 1 online resource (iv, 234 pages) |
| Collana | Gottingen Series in Biophysics |
| Disciplina | 574.8734 |
| Soggetti | Cytoplasmic filaments |
| Lingua di pubblicazione | Inglese |
| Formato | Materiale a stampa |
| Livello bibliografico | Monografia |
| 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 |

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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.

2. **Record Nr.** UNINA9910980045403321
Titolo Sedatives and Hypnotics: Overview

Pubbl/distr/stampa MyJoVE Corporation

Lingua di pubblicazione Inglese

Formato Videoregistrazione

Livello bibliografico Monografia