migration of tumor cells to neighbouring tissue as well as in metastasis to dis-
tant sites in the body via newly formed blood vessels (angiogenesis). We inves-
tigated CXCR4- SDF1α mediated chemotaxis in mouse fibroblasts in an inte-
grated approach from the tissue to the single-molecule level. First, we charac-
terized cellular migratory potential upon stimulation with SDF1α in wound healing assays applying phase contrast microscopy. We find that tran-
siently transfected cells expressing CXCR4 double their migration speed in
comparison to wild type 3T3 cells. Second, we applied single-molecule fluores-
cence microscopy to study the mobility of the G protein-coupled receptor
CXCR4- SDF1α in individual cells and upon stimulation with SDF1α. Two fractions
of receptors prior to stimulation were identified: half of the receptors were im-
mobile while the other half exhibited free diffusion with D ~ 0.3 μm²/s on short
timescales (up to 100 ms). At longer timescales receptors showed confined dif-
fusion within micrometer domains. Global stimulation with SDF1α switched a
subset of the receptors from the immobile to the mobile fraction. We predict
that the impact of a SDF1α gradient might lead to asymmetric receptor diffu-
- sion and subsequently polarized cell behaviour as seen in the wound healing
assays.

114-Plat Quantitative Description of Signaling Downstream of Gq-Coupled Recep-
tors: Similarities and Differences in the Responses of IP3, Calcium, DAG,
PKC, and PIP2
Eamonn J. Dickson, Björn H. Falkenburger, Bertil Hille
University of Washington, Seattle, WA, USA.
Gq-coupled plasma membrane receptors modulate cellular functions by
activating phospholipase C (PLC), which hydrolyses the membrane lipid
phosphatidylinositol (4,5)-bisphosphate (PIP2) into the second messengers
inositoltrisphosphate (IP3) and diacylglycerol (DAG). To better understand the
mechanisms that govern these partially independent signals we monitored
in single, living tsA-201 cells levels of PIP2, IP3, calcium, DAG, and PKC
by optical probes and current. We compared (i) activation of (low-abundance)
endogenous purinergic receptors and oversaturated M1 muscarinic receptors,
and (ii) different concentrations of the muscarinic agonist oxotremorine-M
(oxo-M). Whereas the peak responses from reporters of IP3 (LIBRA/III) and
DAG (CI domains of PKCy) scale with abundance of receptor or agonist,
downstream production of calcium (Fura4F) and PKC activation (CKAR) do not.
Amplitude and duration of calcium signals elicited by 100 μM UTP,
10 nM oxo-M, or 10 μM oxo-M are almost identical. The only difference is a
shorter latency with 10 μM oxo-M. These data suggest that a relatively low
amount of IP3 is required for calcium release. This interpretation is supported
by the finding that a full-size calcium response can still be elicited after PIP2 is
depleted by recruiting a PI 5-phosphatase to the plasma membrane (by rapamy-
-cin-induced dimerization). Duration and late recovery time courses are differ-
ent between IP3 (duration=68 s; τoff =55 s) and calcium (duration=110 s;
τoff=34 s), suggesting that once a threshold of IP3 is reached, the calcium signal
unfolds. Therefore we conclude that the IP3 requirement for calcium release
must be low. The time point and IP3 level (from LIBRA/III) at which the cal-
- cium response starts can provides an estimate of this IP3 threshold. Supported by
NIH grants NS08174 & GM03913 and the HFSP.

115-Plat Vitamin A as an Activator and Sensitizing Chromophore for Rhodopsin
Sadaharu Miyazono, Tomoki Isayama, Clint L. Makino
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MA, USA.
Absorption of light by rhodopsin isomerizes its 11-cis retinal chromophore to the
all-trans conformation. The rhodopsin then activates a biochemical cascade
that produces an electrical response by the photoreceptor. Eventually, all-trans
retinal dissociates from the opsin and is reduced to vitamin A. The truncated re-
- tinal analog, beta-ionone, can pharmacologically activate some types of visual
pigment, mimicking the effects of light. Beta-ionone is not normally found in
the retina, however, vitamin A is present within the photoreceptor and can reach
millimolar concentrations after exposure to bright light. Can vitamin A activate
rhodopsin? In suction electrode recordings from isolated green-sensitive rods of
salamander, exogenous vitamin A decreased circulating current and flash sensi-
tivity of muscle, which are a unique combination of strength, extensibility and
resilience. Single-molecule atomic force microscopy (AFM) studies demon-
stated that the macroscopic behaviour of titin in intact myofibrils can be recon-
stituted by combining the mechanical properties of these mechanical elements
measured at the single-molecule level. Here we report artificial elastomeric
proteins that mimic the molecular architecture of titin through the combina-
tion of well-characterized protein domains GB1 and resilin. We show that these
artificial elastomeric proteins can be photochemically crosslinked and cast
- into solid biomaterials. These biomaterials behave as rubber-like materials
showing high resilience at low strain and as shock-absorber-like materials at
high strain by effectively dissipating energy. These properties are comparable
to the passive elastic properties of muscles within the physiological range of
sarcomere length and so these materials represent a new muscle-mimetic bio-
material. The mechanical properties of these biomaterials can be fine-tuned by
adjusting the composition of the elastomeric proteins, providing the opportu-
nity to develop biomaterials that are mimetic of different types of muscles.
We anticipate that these biomaterials will find applications in tissue engin-
ering as scaffold and matrix for artificial muscles.

111-Plat Viscoelasticity of Globular Proteins Measured from the AC Susceptibility
Yong Wang, Giovanni Zocchi
UCLA, Los Angeles, CA, USA.
We introduce a new method to measure the elasticity and internal viscosity of nanometer
size biological molecules such as globular proteins. Gold nanoparticles, tethered to
a gold surface by the protein, are driven by an AC electric field while
their displacement is synchronously detected by evanescent wave scattering, yielding the
mechanical response function of the macro-
- molecular sample in the frequency domain. We apply the method to measure the both
the elastic constant and internal viscosity of proteins.

116-Plat Designed Biomaterials to Mimic the Passive Elastic Properties of Muscles
Shanshan Li, Yi Cao, Daniel Dudek, John Gosline, Hongbin Li
University of British Columbia, Vancouver, BC, Canada.
The passive elasticity of muscle is largely governed by the I-band part of the
giant muscle protein titin, a complex molecular spring composed of a series of
individually folded immunoglobulin-like domains as well as largely unstruc-
tured unique sequences. These mechanical elements have distinct mechanical
properties, and when combined, they provide the desired passive elastic prop-
erties of muscle, which are a unique combination of strength, extensibility and
resilience. Single-molecule atomic force microscopy (AFM) studies demon-
strated that the macroscopic behaviour of titin in intact myofibrils can be recon-
stituted by combining the mechanical properties of these mechanical elements
measured at the single-molecule level. Here we report artificial elastomeric
proteins that mimic the molecular architecture of titin through the combina-
tion of well-characterized protein domains GB1 and resilin. We show that these
artificial elastomeric proteins can be photochemically crosslinked and cast
- into solid biomaterials. These biomaterials behave as rubber-like materials
showing high resilience at low strain and as shock-absorber-like materials at
high strain by effectively dissipating energy. These properties are comparable
to the passive elastic properties of muscles within the physiological range of
sarcomere length and so these materials represent a new muscle-mimetic bio-
material. The mechanical properties of these biomaterials can be fine-tuned by
adjusting the composition of the elastomeric proteins, providing the opportu-
nity to develop biomaterials that are mimetic of different types of muscles.
We anticipate that these biomaterials will find applications in tissue engin-
ering as scaffold and matrix for artificial muscles.

117-Plat Influenza Virus Adhesion to Living Cells Measured by Single Virus Force
Spectroscopy (SVFS) and Force Probe MD Simulation
Christian Sieben1, Christian Kappel1, Anna Wozniak2, Rong Zhu4,
Christian Rankl1, Peter Hinterdorfer4, Helmut Grubmüller1,
Andreas Herrmann1
1Humboldt-University Berlin, Berlin, Germany, 2Max Planck Institute for
Biophysical Chemistry, Göttingen, Germany, 3JKP Instruments AG, Berlin,
Germany, 4Johannes Kepler University Linz, Linz, Austria.
Influenza virus belongs to a wide range of viruses that are enclosed in a lipid
envelope. The major spike protein of the viral envelope hemagglutinin (HA)
binds sialic acid (SA) residues of glycoproteins on the plasma membrane of

PLATFORM I: Molecular Mechanics & Force Spectroscopy I

1, Christian Kappel2, Anna Wozniak3, Rong Zhu4,
Christian Rankl1, Peter Hinterdorfer4, Helmut Grubmüller2,
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1Humboldt-University Berlin, Berlin, Germany, 2Max Planck Institute for
Biophysical Chemistry, Göttingen, Germany, 3JKP Instruments AG, Berlin,
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Influenza virus belongs to a wide range of viruses that are enclosed in a lipid
envelope. The major spike protein of the viral envelope hemagglutinin (HA)
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