microenvironment. The fluid flux through the membrane is governed by the dif-
ference of chemical potential across the membrane. The osmotic pressure is ob-
tained from the ion diffusion and flux and the hydrostatic pressure is obtained
from the fluid dynamics inside the cell. The flux of cations and anions across the
cell membrane is determined by the properties of the ion channels as well as the
external electric field. Results show that without the contribution from actin
network and myosin contraction, water permeation can also drive non-
polarized cells with the presence of an external electric field. The direction
of migration is affected by the properties of ion channels which are cell-type
dependent. The results suggest that external voltages can be used to sort cells.

2303-Pos Board B440
Circular Dorsal Ruffles Increase Directional Persistence of Cell Migration by Actin Diffusion from Ruffles to Lamellipodia
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Circular dorsal ruffles (CDRs) are transient actin structures which have been
linked to cell motility but the exact mechanism is still unclear. CDRs appear
and grow in size after cells are stimulated with growth factors, such as the
platelet-derived growth factor, eventually disappearing tens of minutes after
stimulation. The role of CDR formation in cell motility is investigated for
NIH 3T3 fibroblasts seeded on compliant polyacrylamide substrates. We found
that CDR formation increases cell migration directional persistence but did not
affect cell migration speed. Furthermore, an increased incidence in the loco-
mentum protrusion at the cell edge in the vicinity of the CDRs was observed.
Relocalization of lamellipodia occurred 1 to 6 min after CDR forma-
tion at the cell edge closest to the site of CDR formation. The time lag between
peak CDR formation and the peak lamellipodial protrusion is then correlated
with the spatial distance between the CDR and the lamellipodia; this time scale
is consistent with the diffusive time scale of cytosolic globular actin (G actin).
Using green to red photowritable Dendra2-conjugated actin, we photocon-
verted CDR actin from green to red and observed the subsequent appearance
of red fluorescent actin in the lamellipodia at the cell leading edge. These find-
ings help shed light on the interconversions between mesoscopic actin struc-
tures in cell behavior.

2304-Pos Board B441
Modeling Transmigration of Malaria Infected Red Blood Cells through Inter-
endothelial Slits in Human Spleens using Dissipative Particle Dynamics
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We simulate the transmigration of malaria-infected red blood cells (RBCs)
through the inter-endothelial slits in the human spleen by using Dissipative Par-
ticle Dynamics based two-component RBC model. We modeled the spectrin-
actin network and the lipid bilayer separately and considered the real number
of the structural proteins in the model. The mechanical properties of the
bilayer- cytoskeleton interactions, such as stiffness and friction, are calibrated
by comparing with membrane fluctuations and tank-treading experiments. First,
we further validated our numerical model by comparing the predicted retention
rates of healthy and pathological cells in an ‘artificial spleen’ consisting of micro
environments. The fluid flux through the membrane is governed by the dif-
ference of chemical potential across the membrane. The osmotic pressure is ob-
tained from the ion diffusion and flux and the hydrostatic pressure is obtained
from the fluid dynamics inside the cell. The flux of cations and anions across the
cell membrane is determined by the properties of the ion channels as well as the
external electric field. Results show that without the contribution from actin
network and myosin contraction, water permeation can also drive non-
polarized cells with the presence of an external electric field. The direction
of migration is affected by the properties of ion channels which are cell-type
dependent. The results suggest that external voltages can be used to sort cells.

2305-Pos Board B442
Restricted Exchange Environment Chambers for Creating and Manipu-
lating Diffusive Gradients in 2D Cell Culture
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Diffusive exchange between capillaries and the tissues they serve generates concentration gradients of a significant number of soluble molecules, creating
heterogeneous microenvironments on the length scale of single cells. This
heterogeneity is not well captured in 2D cell culture models, and it is not
easily controlled or studied in 3D systems. Here we describe a simple
chamber in which diffusive gradients similar to those found in vivo can be
created and manipulated. In restricted exchange environment chambers (RE-
ECs), cells are grown in a narrow gap formed by two coverslips, and dif-
usive exchange occurs via one or more small openings machined into one
coverslip – through which the cells exchange nutrients and metabolic waste
with the bulk medium. Based on a concept similar to the sandwich assay
(Hallmark and Alpen, Cell Tissue Kinet 18:597, 1985) and compatible with
multiwell plate formats used in high-throughput investigations, REECs
improve experimental control of gradient structure in cell culture. Because
diffusive concentration gradients vary as a function of distance from a source
or sink, the dimensions of the chamber (e.g. height of the gap) and the num-
ber, shape, and size of openings create the gradient structure. For example, in
REECs with a single round opening (order 200 μm diameter), concentration
gradients form radially. Only cells within a several hundred micrometers of
the opening exchange sufficient metabolites to survive - similar to diffusive
exchange near a capillary in a tissue. Alternatively, cells cultured in REECs
with two parallel bar-shaped openings produce the 1-dimensional equivalent
of a spheroid. Using these restricted exchange environment chambers, we find
that fibroblasts align themselves along the axis of diffusion while MDCK
cells do not. MDCK cells do, though, exhibit morphological variations along
the diffusive gradient.

2306-Pos Board B443
Coupling a Mechanosensitive Channel with a Vesicle under Shear Flow
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Mechanosensitive channels enable cells to respond to their local environment.
Continuous mechanical stimulation has been proposed to describe how bilayer
def ormation induced by the transmembrane protein and the membrane tension
affect free energy of channel gating under static conditions. The dy-
namics of mechanosensitive channels under shear flow conditions however
remains largely unexplored. Cells under flow display interesting features not
observed under static environments. Here we present a model coupling a mechanosen-
tive channel with the dynamics of a vesicle under shear flow to investigate how
the channel gating responds to hydrodynamic stress. The model could be used
to investigate the release of signaling molecules, transport of ions or drugs
across cell membranes under flow in biological systems, as well as the design
and control of channel gating in synthetic cells.

2307-Pos Board B444
Perturbing the Active Process of Hair Cells: Self Recovery of Spontaneous
Oscillations Following Overstimulation
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In the inner ear, hair cells perform the transduction of mechanical input into
electrical output. An energy-consuming process enhances their sensitivity to
incoming auditory and vestibular stimuli. One manifestation of this active pro-
cess is spontaneous oscillation of the mechano-sensitive organelle, the hair
bundle, which is at the apical surface of each hair cell. To attain this increased
sensitivity, the hair bundle is postulated to operate near a bifurcation, where an
internal control parameter vital to the active process determines whether the
bundle shows limit cycle oscillations or is quiescent. This control parameter
may be linked to adaptation in vertebrate hair cells and could help explain
how prolonged high-level sounds cause a temporary threshold shift in mamma-
lian hearing. High amplitude, prolonged deflection of bullfrog sacculus bundles
have been shown to temporarily suppress spontaneous oscillations, suggesting
a readjustment of the control parameter through a bifurcation. The transition
back from quiescence to limit cycle oscillations has been shown to depend on
the duration of the imposed deflection and on calcium ion concentration
around the mechanically gated transduction channels.
Here, we present experiments where we identify other environmental factors
that affect this control of the active process. We introduce various pharmaco-
logical agents to manipulate the mechano-sensitive transduction channels and
the myosin motors inside the hair bundles. We compare how these agents affect
particular components of the internal control parameter by measuring the dur-
tion of the induced quiescent intervals and the time scales associated with the
return of the bundle’s position to equilibrium. Additionally, we attach magnetic
bead particles to the hair bundles and deflect with a strong magnetic field. Thus,
hair bundles avoid physical contact with the stimulus probe, and experience no
external hydrodynamic effects. Selected results are discussed.