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Case Studies on Inflammation and Mechanotransduction notes

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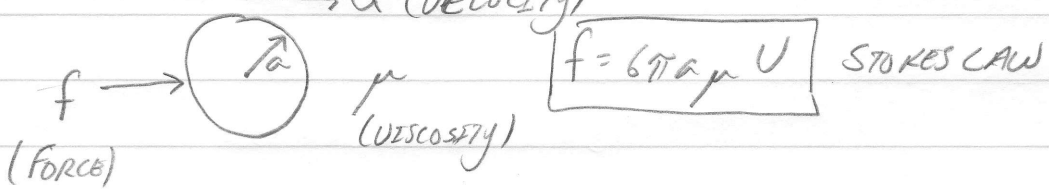
GEM 4 8/15/06

CONTINUATION FROM MORNING SESSION

FLUCTUATION DISSIPATION THEORY

→ TRACK CENTROID OF BEAD ATTACHED TO CELL SURFACE

BEADS "STALL AND HOPS"



MEAN FREEPATH

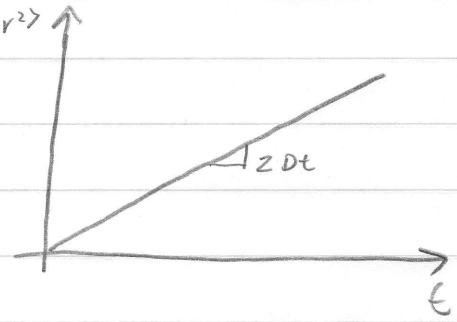
$D = \ell^2/\tau$ ← MEAN FREE TIME

↑ DIFFUSION CONSTANT

$$\frac{1}{2} m \langle U^2 \rangle = \frac{1}{2} K_B T \implies 6\pi a \mu D = K_B T$$

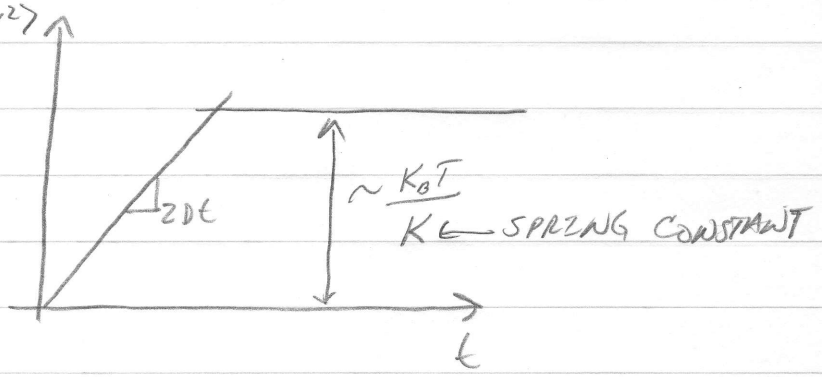
EXAMPLE : $M_w \sim a^3$, $D \sim M_w^{-1/3}$ ⇒ TRUE IF $M_w > 1000$

EXAMPLE : $\mu = K_B T / 6\pi a D$



EXAMPLE3: GENERALIZED (MASON & WEITZ, 1995)

DIFFUSION ⇒ VISCOELASTIC MEDIA AT THERMODYNAMIC EQ.



$$\pi a s G(s) \langle \Delta r^2(s) \rangle = K_B T$$

$$\underbrace{F(\omega)}_{\text{AGITATION}} = \underbrace{2K_BT\,G''(\omega)/\omega}_{\text{THERMAL HITS}} + \underbrace{\Delta(\omega)}_{\text{MOTOR HITS}}$$

$\Delta(\omega) \sim \omega^{-\gamma}$ $(\gamma = 2)$

TAKES INTO ACCOUNT OTHER EFFECTS IN CELL (ATP)

$G^* \sim (j\omega)^{x-1}$

FOCAL ADHESION

→ CONNECTION BETWEEN ECM AND CYTOSKELETON

→ CELL CAN SENSE ITS ENVIRONMENT AND RESPOND TO IT.

2D VS. 3D ⇒ CHANGE THE STRUCTURE OF FOCAL ADHESIONS

BIOMECHANICS AT ALL LENGTH SCALES — R.D. KAMM (MIT)

MECHANOTRANSDUCTION ⇒ SENSING FORCE AND CONVERTING IT INTO A BIOCHEMICAL RESPONSE

HOW DOES THIS HAPPEN?

→ NOT COMPLETELY UNDERSTOOD, SEVERAL HYPOTHESES.

FORCE LEVELS FOR MOLECULAR UNFOLDING - UNBINDING : 10 - 100 pN

MOLECULAR DYNAMICS ⇒ SIMULATE WHAT MAY HAPPEN AS FORCES ARE APPLIED TO MOLECULES AND INDUCE CONFORMATIONAL CHANGES

UNDERSTANDING THE PRINCIPLES THAT GOVERN ADAPTIVE IMMUNE SYSTEM — Dr. ARUP CHAKROBORTY (MIT)

T-CELLS ⇒ DEAL WITH PATHOGENS

↳ ORCHESTRATE THE ADAPTIVE IMMUNE SYSTEM

THERE ARE MOLECULAR SIGNATURES INDICATING THE PRESENCE OF PATHOGENS. THESE SIGNATURES CAN BIND TO T-CELL RECEPTORS AND ACTIVATE THE T-CELL RESPONSE.

HOW DOES T-CELL DISCRIMINATE BETWEEN "SELF" AND "NON-SELF"?

T-CELL CAN DETECT 10 ANTIGENS OUT 30,000 ENDOGENOUS MOLECULES

↳ HIGH SENSITIVITY AND SPECIFICITY

COOPERATIVITY BETWEEN ANTIGEN AND ENDOGENOUS PEPTIDES!!

(MODEL)