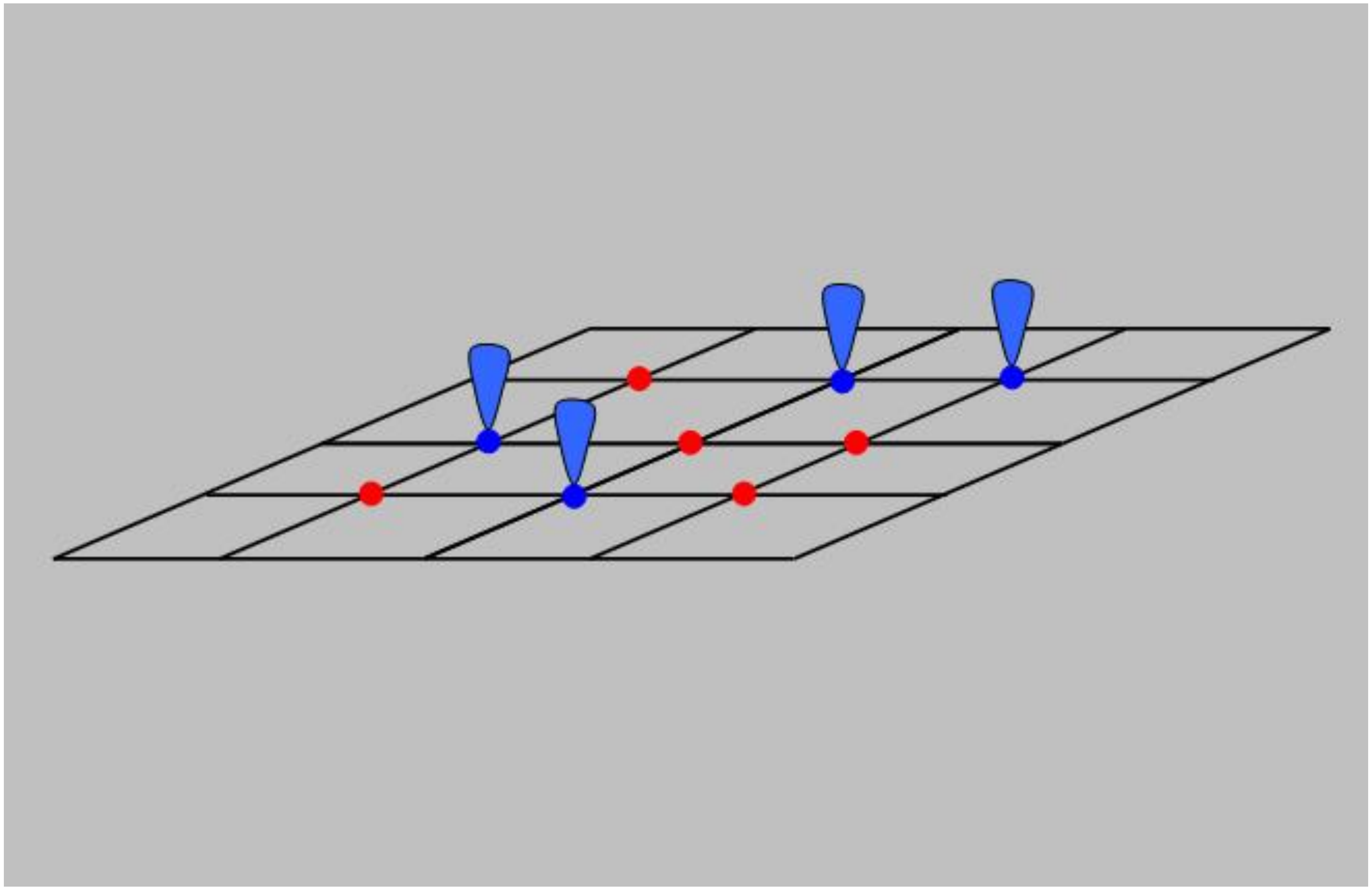
Physics 176/276
Quantitative Molecular Biology

Lecture VII: Dynamics of receptors and allostery

http://physics.ucsd.edu/students/courses/winter2014/physics176

Analogy with adsorption of a gas onto a solid surface

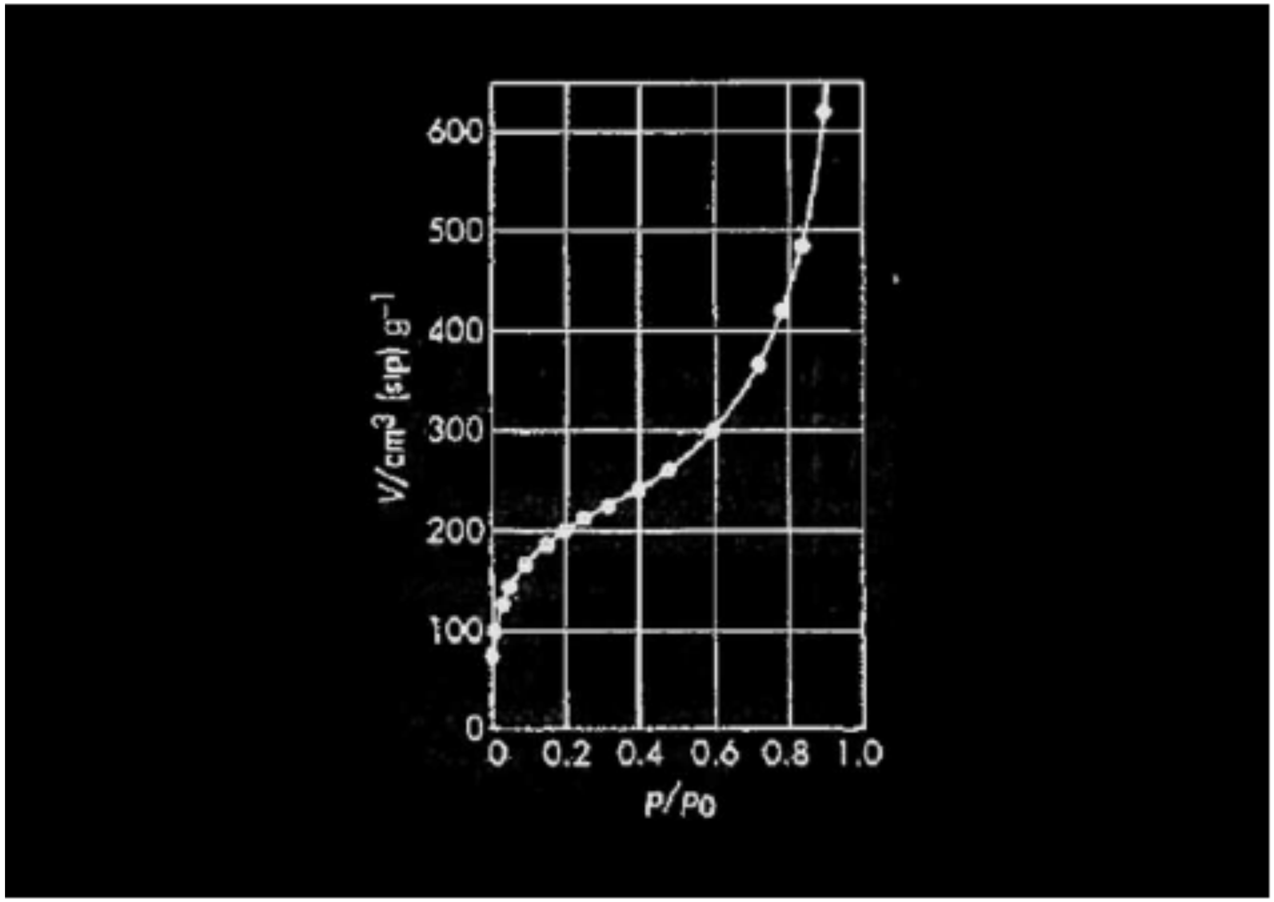


Control parameter in adsorption experiments is pressure (Langmuir law)

$$\langle occupied \rangle = \frac{p}{p + p_*}$$

Control parameter in adsorption experiments is pressure (Langmuir law)

Experimental law for adsorption of N_2 onto silica



Multiple layers of adsorption onto a solid surface

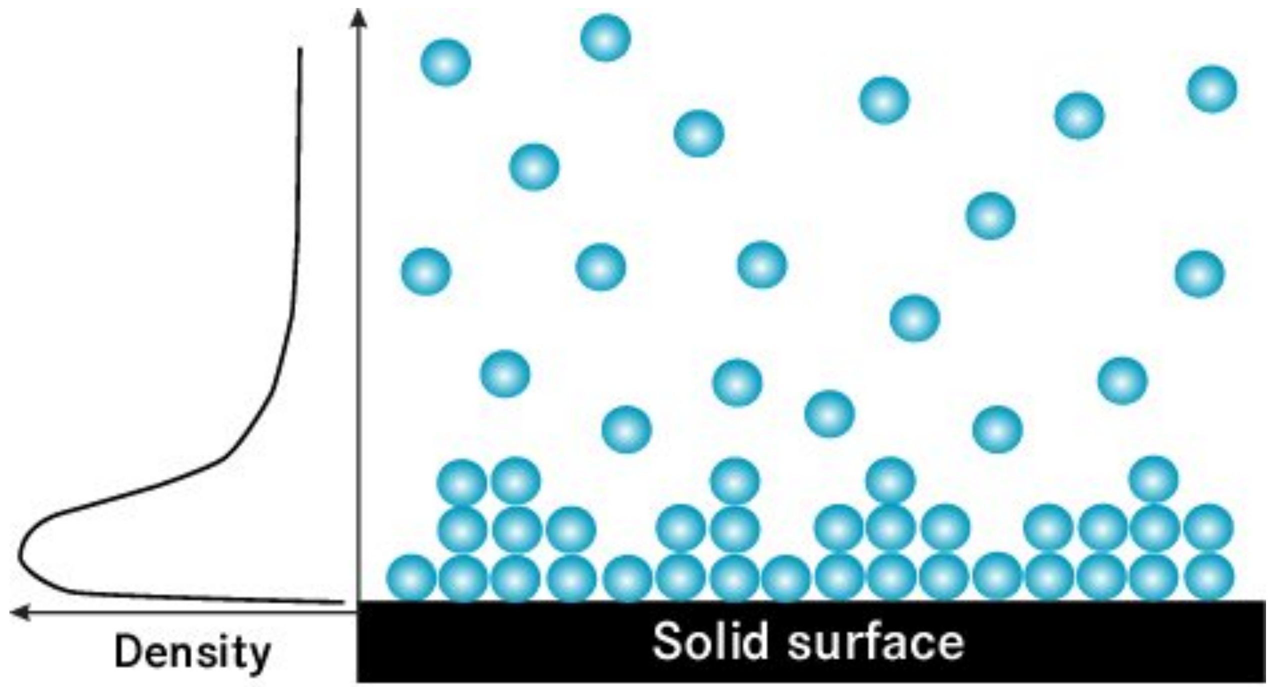
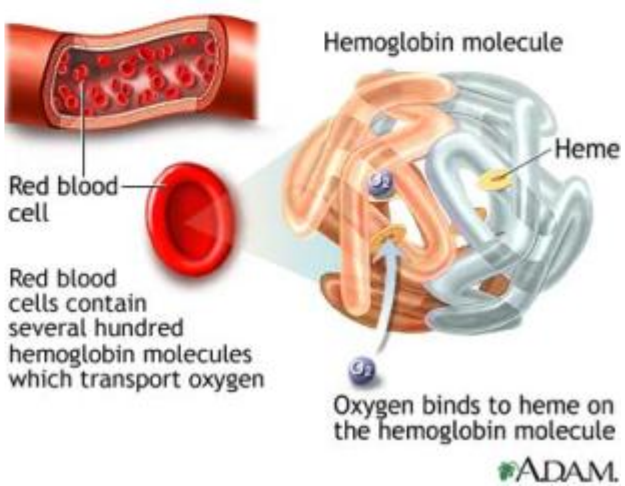
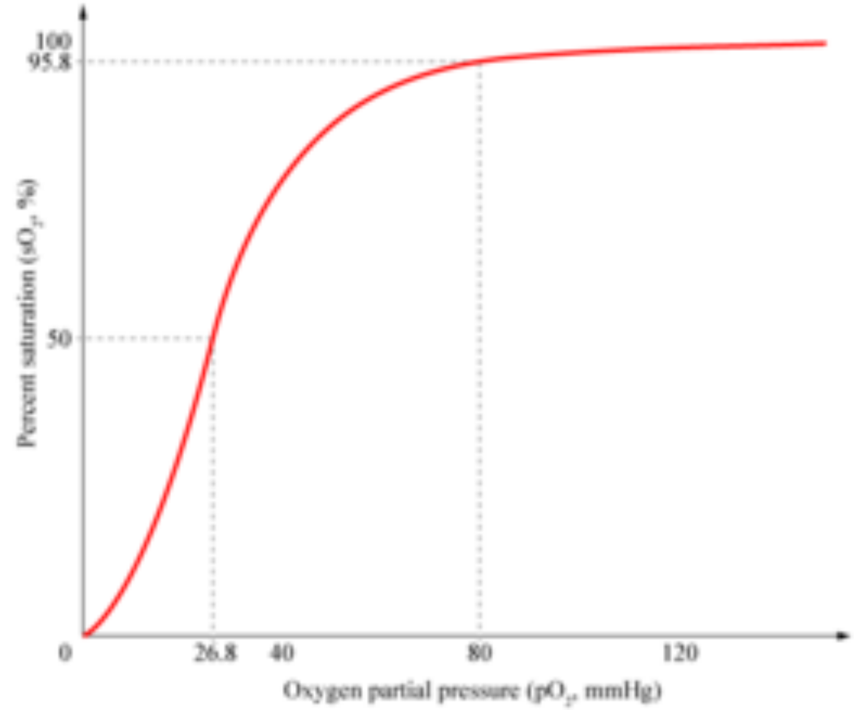


Figure 2: Triple layer adsorption on a solid surface and representation of the density distribution

Brunauer, Emmett et Teller *J. Am. Chem. Soc.*, **60**, 309, (1938)

Sigmoidal uptake of oxygen by hemoglobin

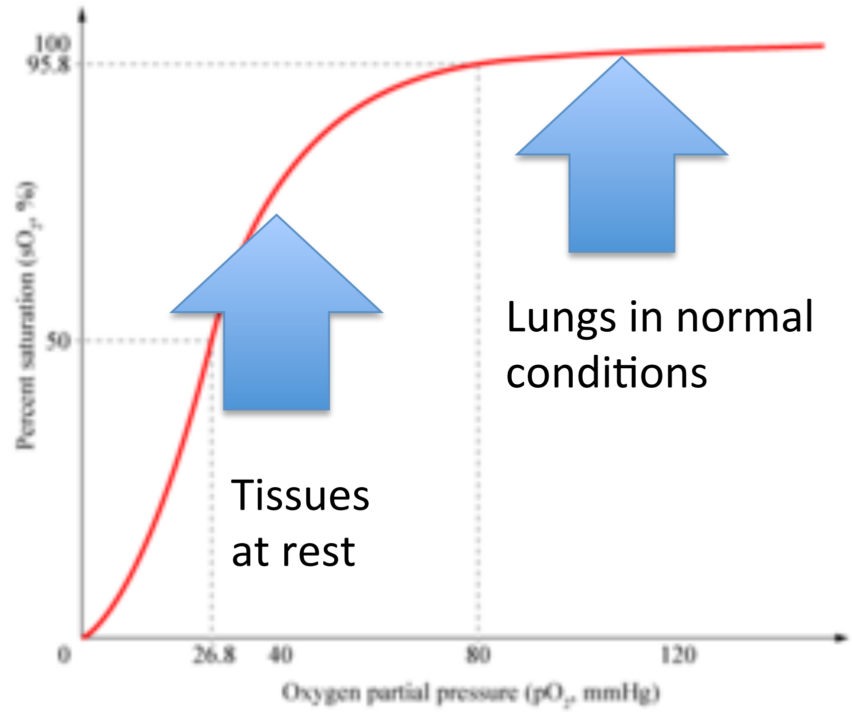


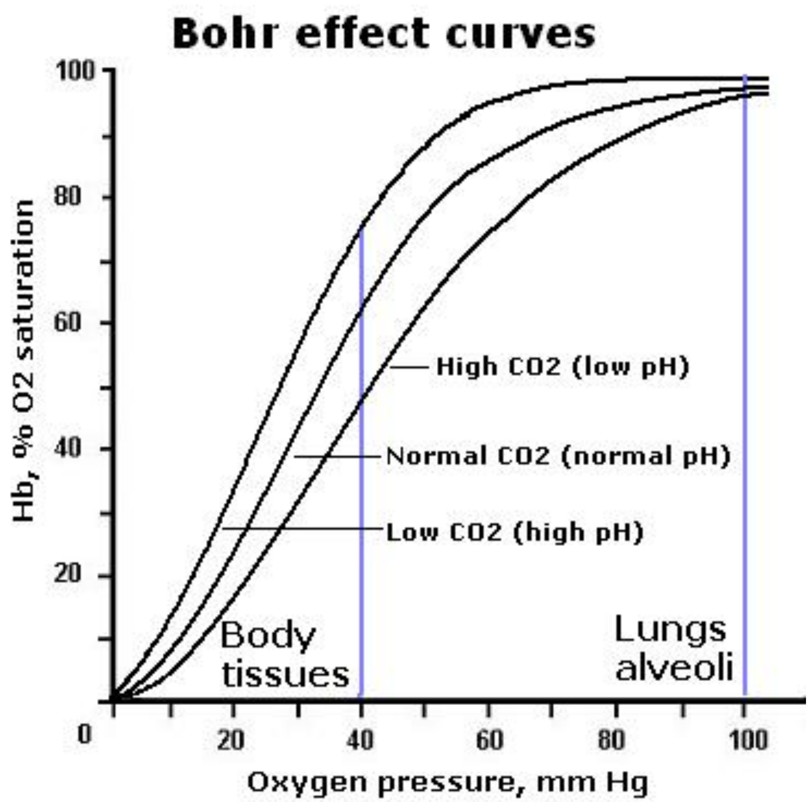


Physiology of respiration

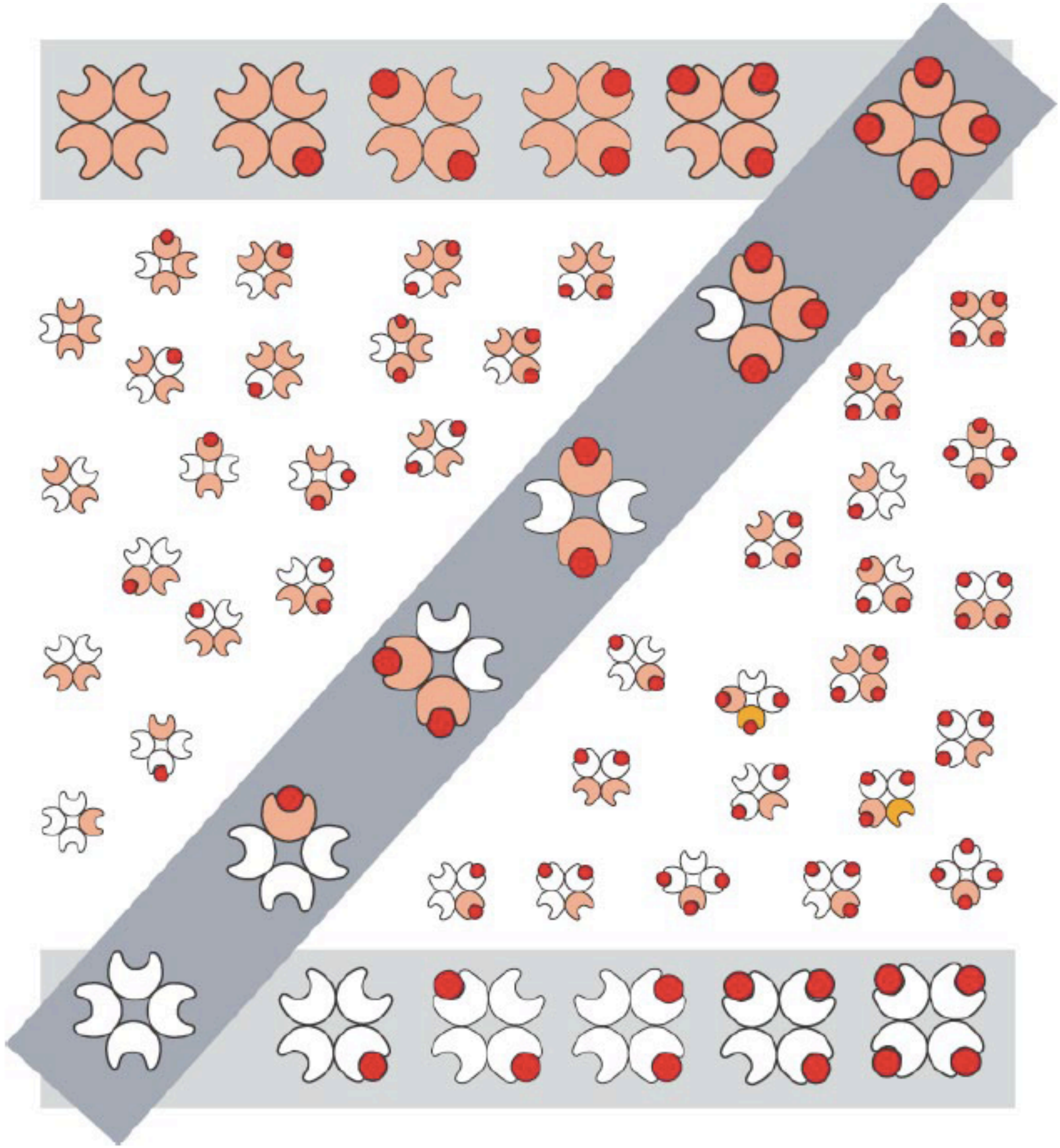
https://www.youtube.com/watch?v=WXOBJEXxNEo&feature=player_embedded

Physiological importance of the sigmoidal shape of the uptake curve





What are the states considered by KNF and those by MWC?



On the Nature of Allosteric Transitions: A Plausible Model

JACQUES MONOD, JEFFRIES WYMAN AND JEAN-PIERRE CHANGEUX

What you got spared!

$$R_0 \longleftrightarrow T_0$$

$$\begin{array}{llll} R_0 + F \longleftrightarrow R_1 & & T_0 + F \longleftrightarrow T_1 \\ R_1 + F \longleftrightarrow R_2 & & T_1 + F \longleftrightarrow T_2 \\ \cdots & & \cdots \\ R_{n-1} + F \longleftrightarrow R_n & & T_{n-1} + F \longleftrightarrow T_n \end{array}$$

Taking into account the probability factors for the dissociations of the $R_1, R_2 \ldots R_n$ and $T_1, T_2 \ldots T_n$ complexes, we may write the following equilibrium equations:

$$T_0 = LR_0$$

$$R_1 = R_0 \, n \frac{F}{K_R} \qquad T_1 = T_0 \, n \frac{F}{K_T}$$

$$R_2 = R_1 \frac{n-1}{2} \frac{F}{K_R} \qquad T_2 = T_1 \frac{n-1}{2} \frac{F}{K_T}$$

$$\cdots \qquad \cdots$$

$$R_n = R_{n-1} \frac{1}{n} \frac{F}{K_R} \qquad T_n = T_{n-1} \frac{1}{n} \frac{F}{K_T}$$

Let us now define two functions corresponding respectively to:

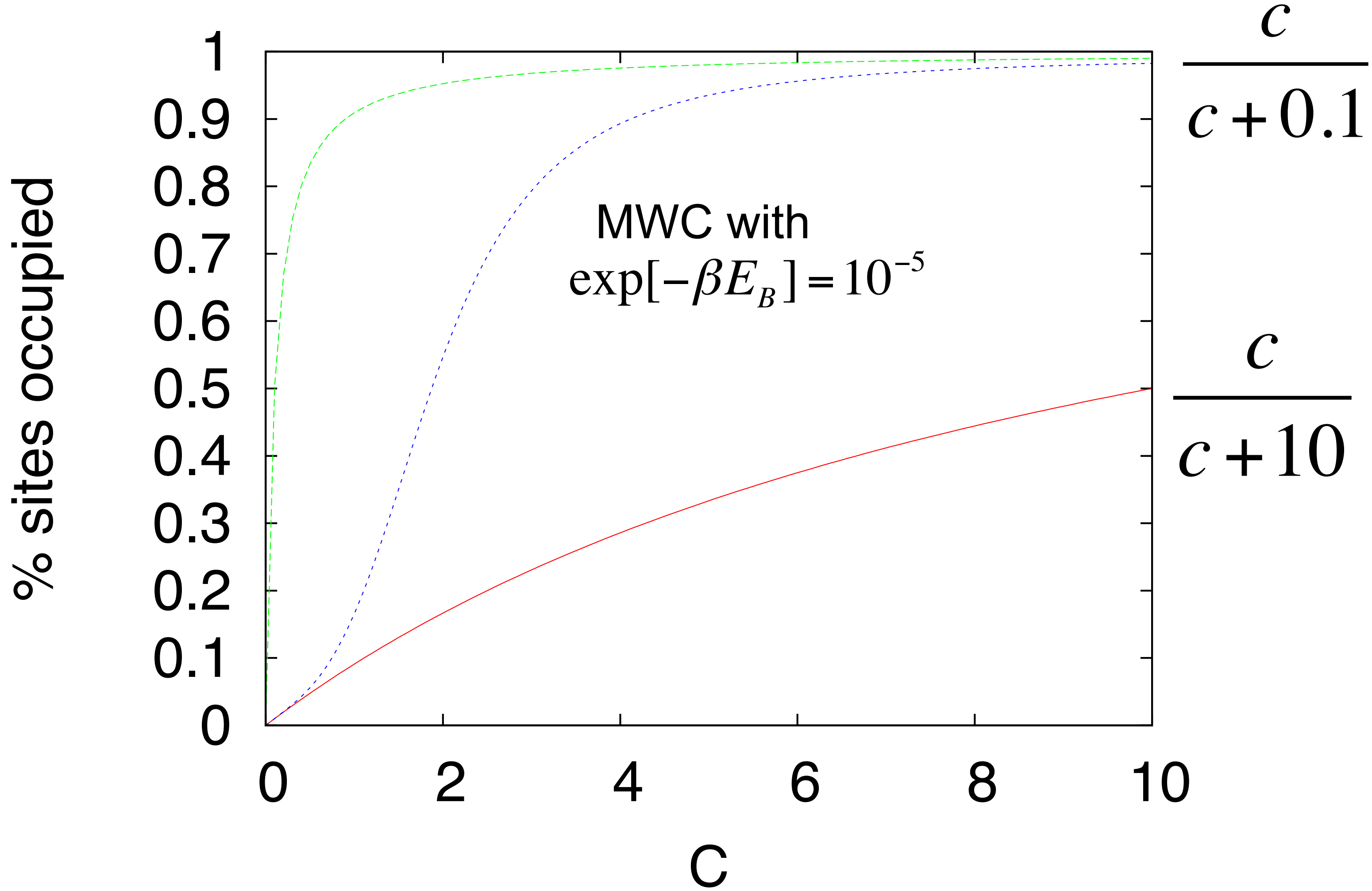
(a) the fraction of protein in the R state:

$$\bar{R} = \frac{R_0 + R_1 + R_2 + \ldots + R_n}{(R_0 + R_1 + R_2 + \ldots + R_n) + (T_0 + T_1 + T_2 + \ldots + T_n)}.$$

(b) the fraction of sites actually bound by the ligand:

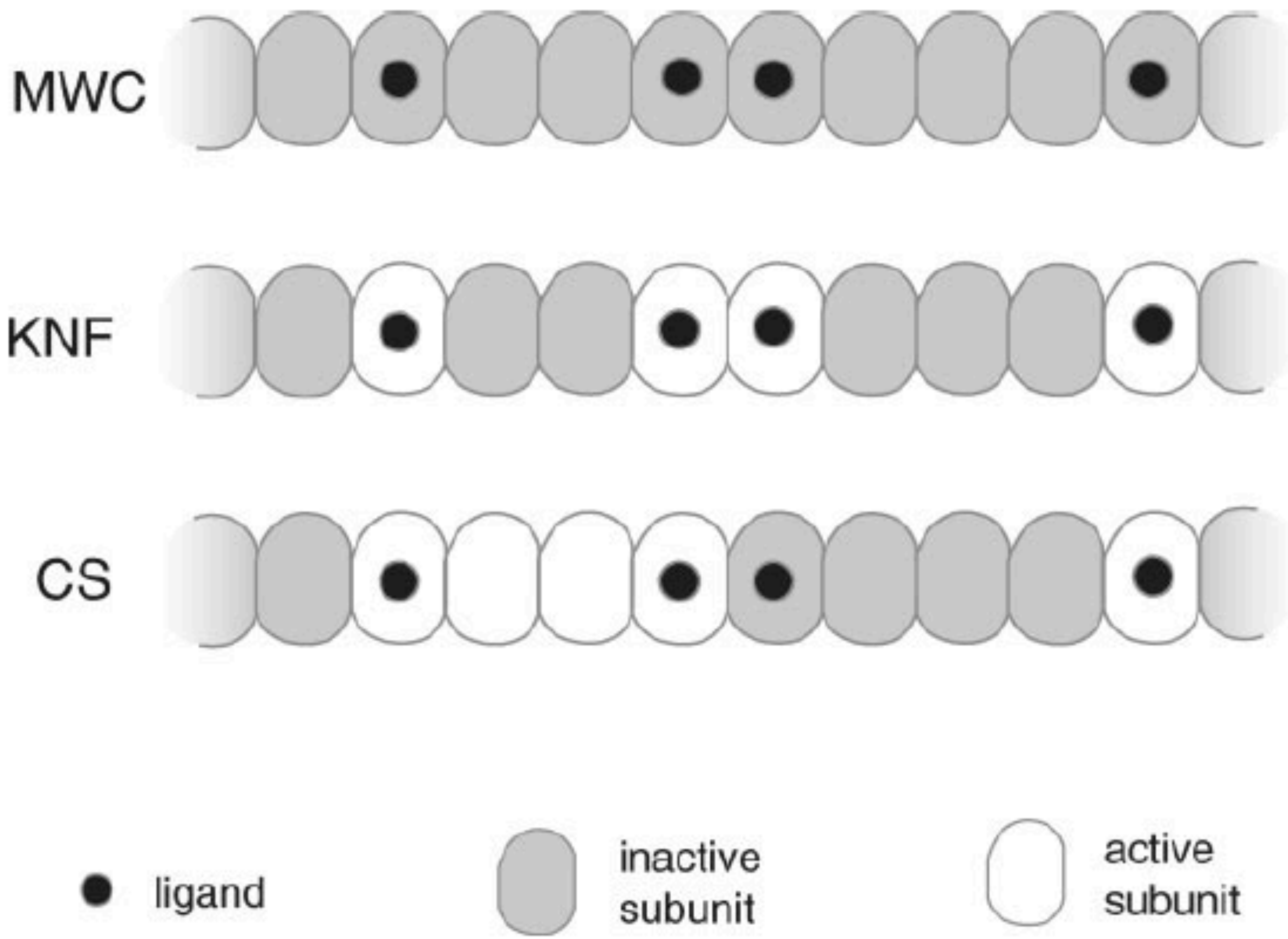
$$\bar{Y}_F = \frac{(R_1 + 2R_2 + \ldots + nR_n) \quad + \quad (T_1 + 2T_2 + \ldots + nT_n)}{n[(R_0 + R_1 + R_2 + \ldots + R_n) + (T_0 + T_1 + T_2 + \ldots + T_n)]}.$$

Example of the behavior for a MWC curve



CONFORMATIONAL SPREAD: Allosteric states in **Multiprotein complexes**

D. Bray
JMB
2013 for
review



The idea is that the points of high susceptibility will amplify small changes of the stimulus (magnetic field) into big changes of the response (magnetization). Systems are finite, so even not a genuine phase transition is sufficient (Duke et al., JMB, 2001).

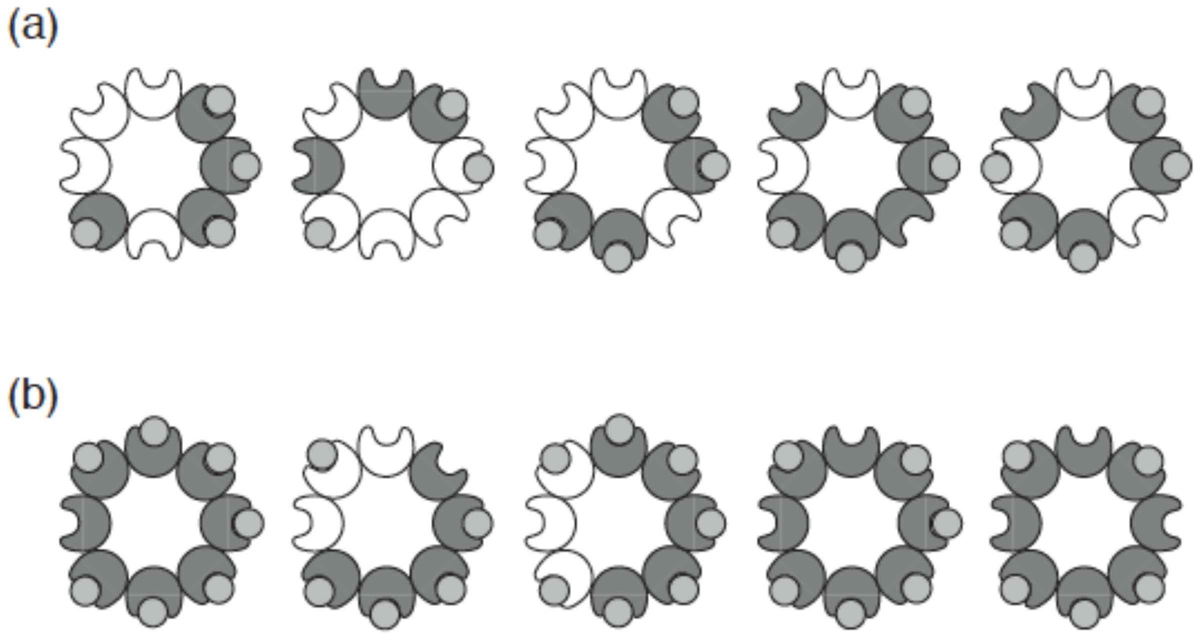
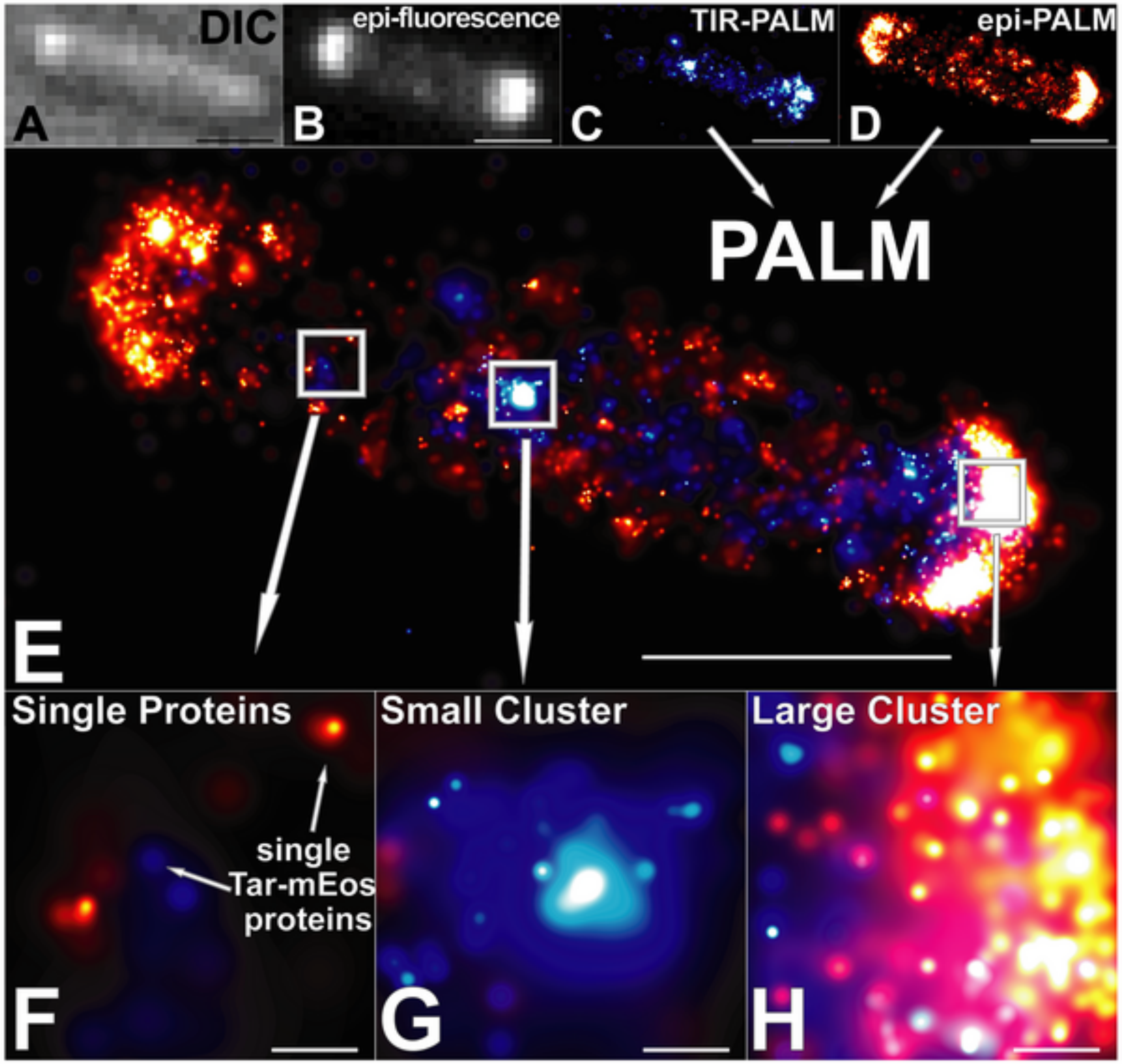


Figure 2. Typical changes in a protein ring. In this example, a ring of eight protomers was chosen and two sequential snapshots of its state are shown in the presence of a concentration $c_{0.5}$ of effector (a concentration leading to 50% occupancy on average). In the first sequence (a) coupling is absent ($E_J = 0$) and the changes in protomers are uncoordinated; in the second (b) strong coupling ($E_J = 2kT$) results in coherent behaviour, with all of the protomers assuming the same state for most of the time.

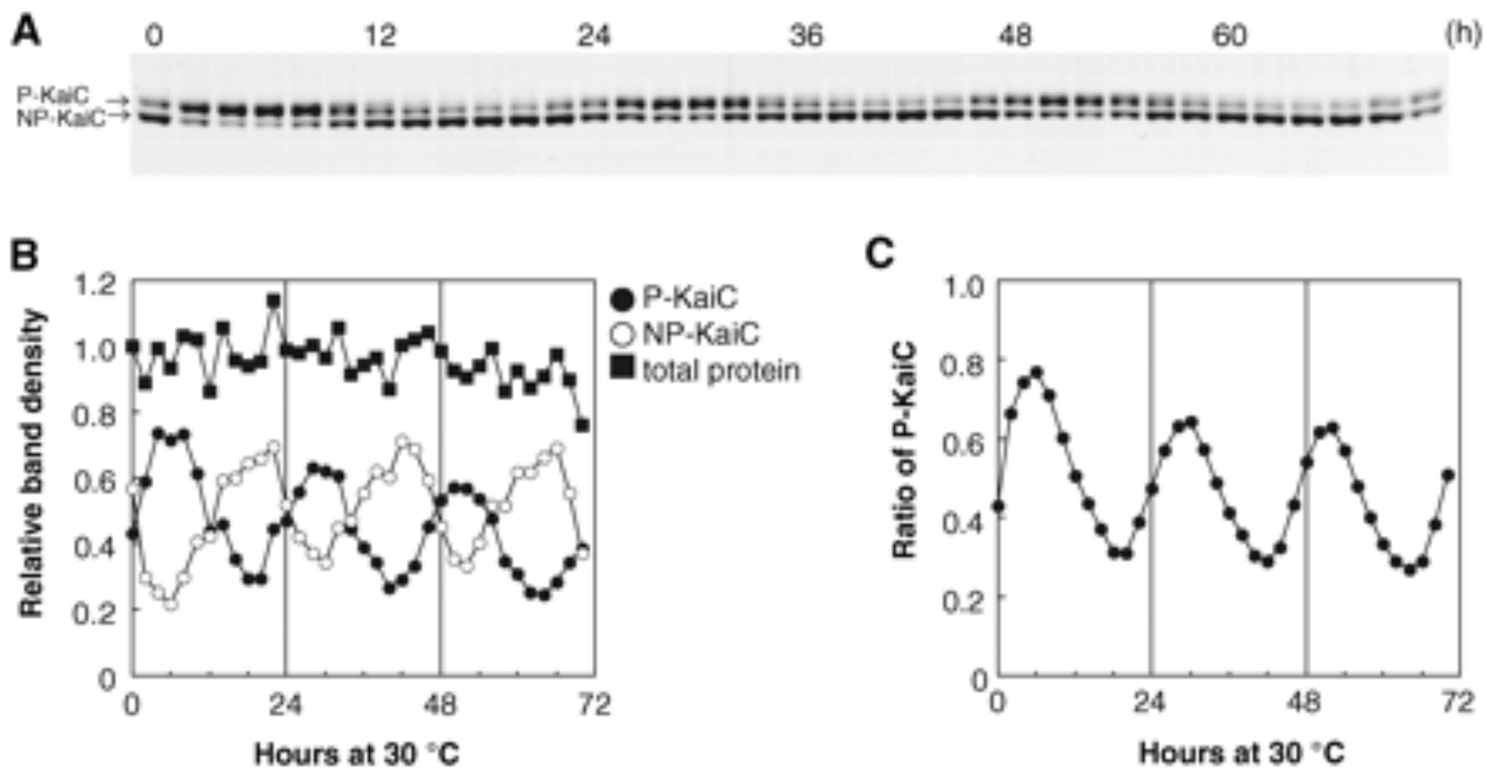
Recent applications to the flagellar motor (Ma et al, PLoS Comp Biol, 2012)

Clusters of Tar receptors (for the aminoacid aspartate)



Circadian cycles in cyanobacteria

Nakajima et al, Science 2005



J.S. van Zon, D.K. Lubensky, P.R.H. Altena and P.R. ten Wolde,
*An allosteric model of circadian KaiC phosphorylation, PNAS **104**, 7420--7425 (2007).*