iBio Seminars Part III: Making Rafts in cell membranes

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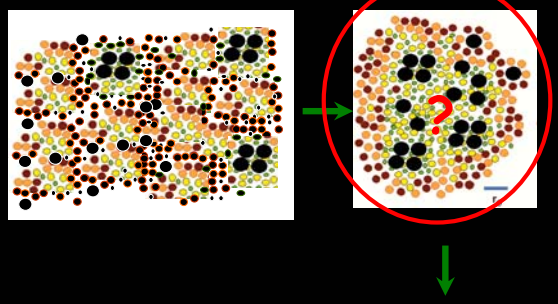
Functional Rafts : A working hypothesis

pre-existing organization induced rafts



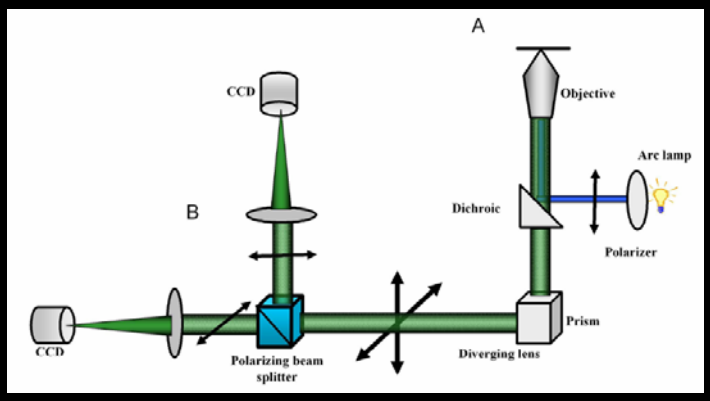
Sorting or Signaling Function

What makes nano-clusters?

What induces functional domains?

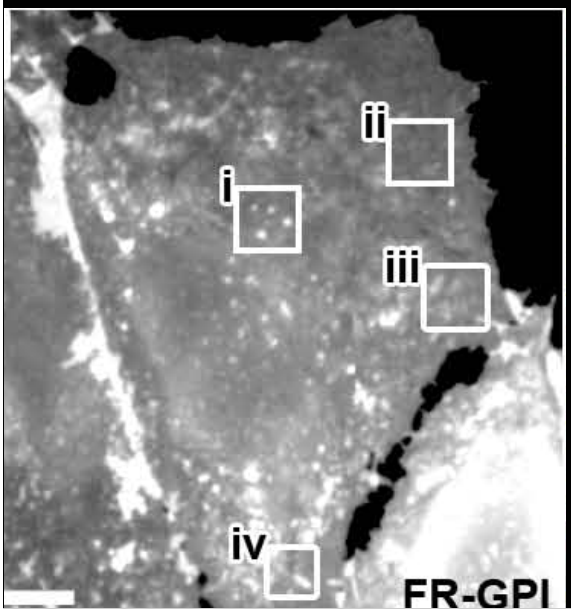
Mayor and Rao, *Traffic* (2004)

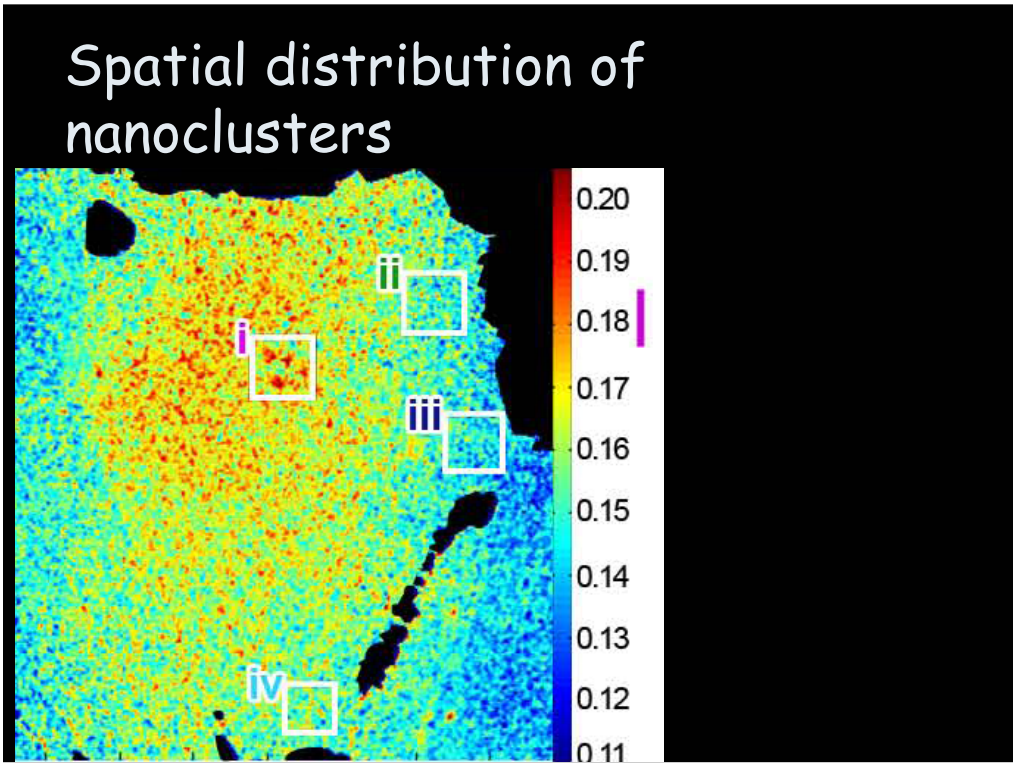
High resolution FRET imaging

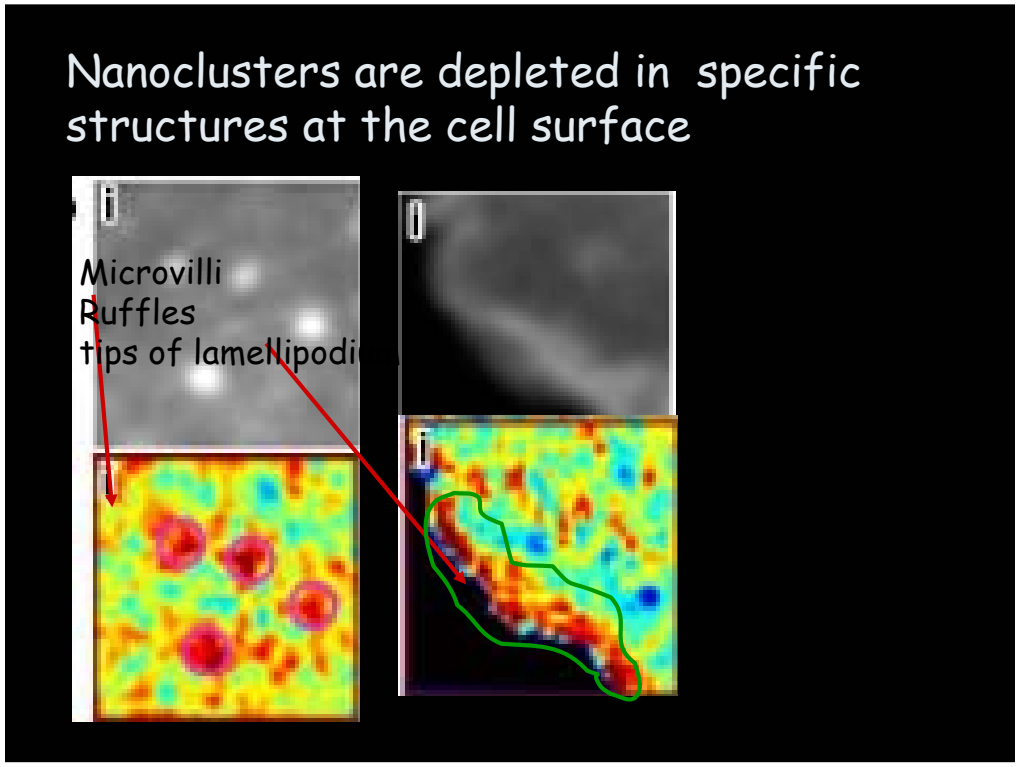


High resolution ~ FRET imaging at 300 nm spatial resolution

Spatial distribution of nanoclusters




Spatial distribution of nanoclusters
i
ii
iii
iv
0.20
0.19
0.18
0.17
0.16
0.15
0.14
0.13
0.12
0.11


Nanoclusters are depleted in specific structures at the cell surface
Microvilli
Ruffles
tips of lamellipodi

Nanoclusters are depleted in ruffles

Depleted of clusters

Microvilli
Ruffles
tips of lamellipodium

Ruffling Movie

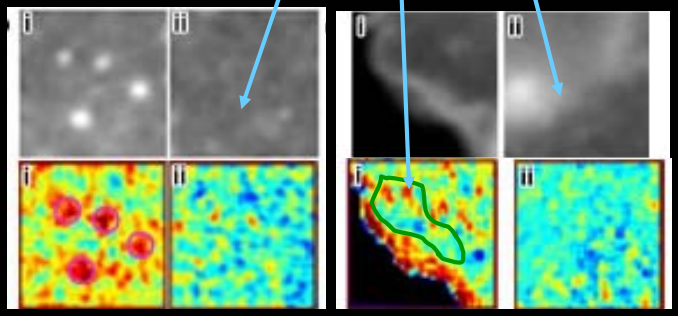
Nanoclusters are enriched in flat regions of cell membranes

Depleted of clusters

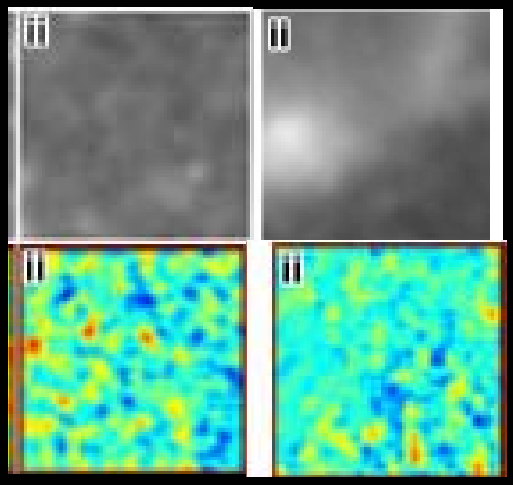
Microvilli
Ruffles
tips of lamellipodium

Enriched in clusters

Flat-cell scapes
lamellum behind lamellipodium



Flat-scapes of the cell membrane exhibit a patchwork of nanocluster-rich regions

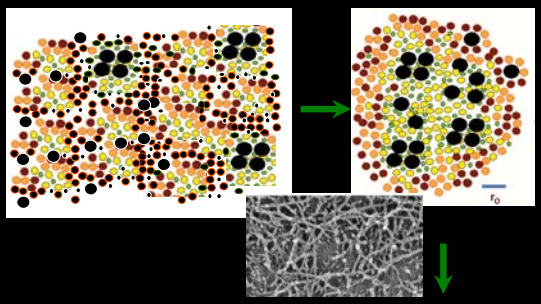


Role of the actin-cytoskeleton in nano-cluster distribution

- Localization of nanoclusters with specific type of actin organization
- Actin perturbation dramatically modifies nanocluster distribution
- Inhibition of actin-polymerization activity, inhibits nanocluster formation and breakup

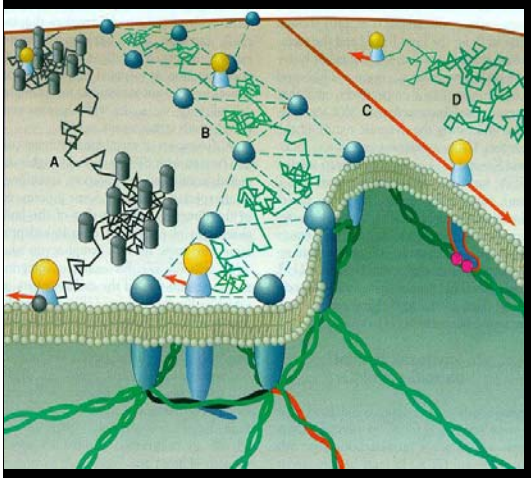
Functional Rafts : A role for actin?

pre-existing organization induced rafts



Sorting or Signaling Function

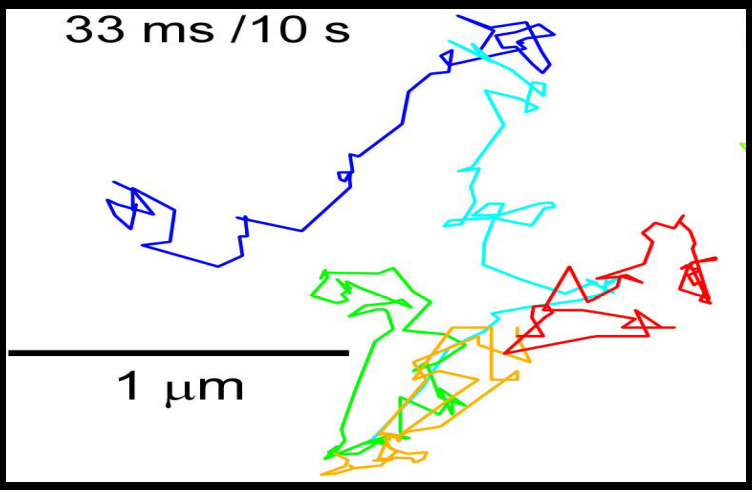
'The supported bilayer'



Jacobson, *Science,* 1999
Ritchie et al. *Mol.Memb. Biol.* 2003

Membrane Skeleton Fence

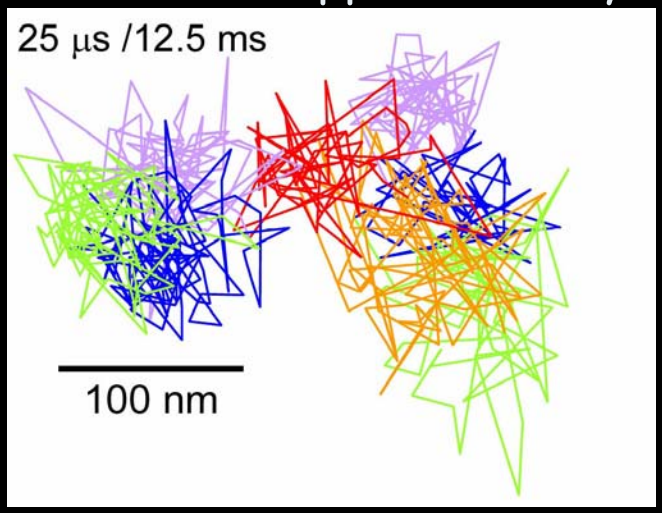
'The supported bilayer'



Jacobson, *Science*, 1999
Ritchie et al. *Mol.Memb. Biol.* 2003

Membrane Skeleton Fence

'The supported bilayer'



Jacobson, *Science,* 1999
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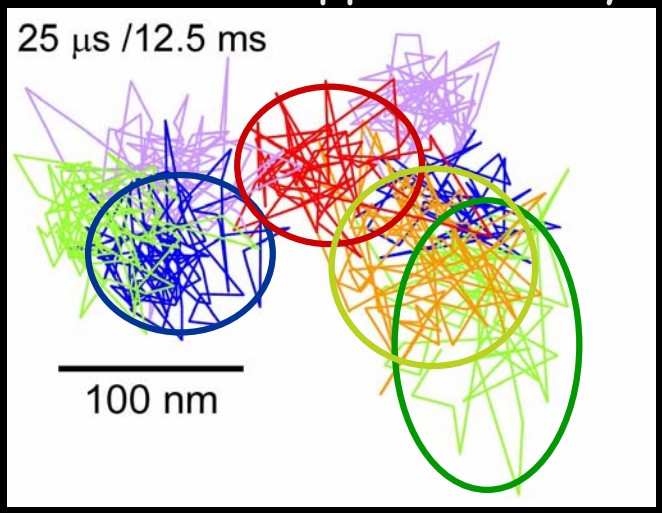
Membrane Skeleton Fence

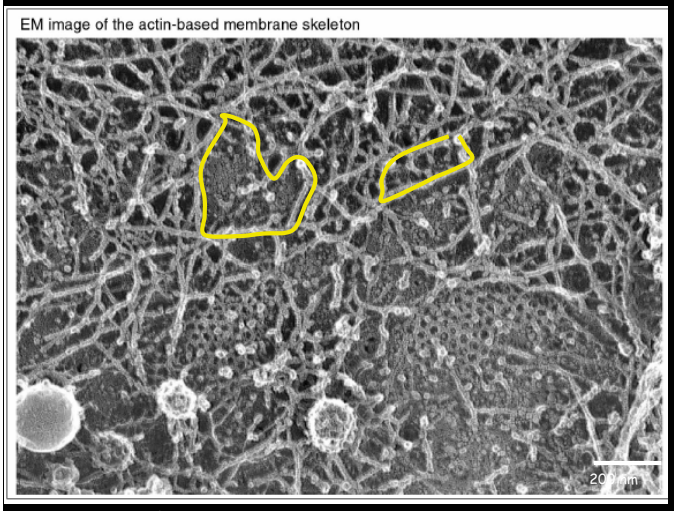
'The supported bilayer'



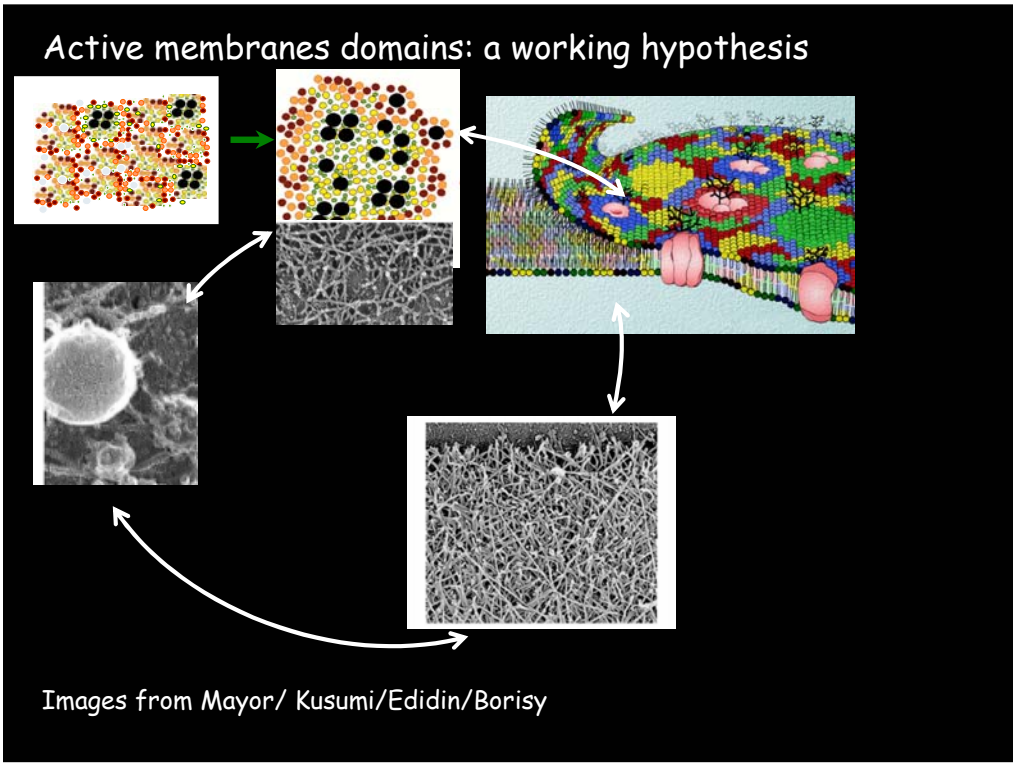
Jacobson, *Science,* 1999
Ritchie et al. *Mol.Memb. Biol.* 2003

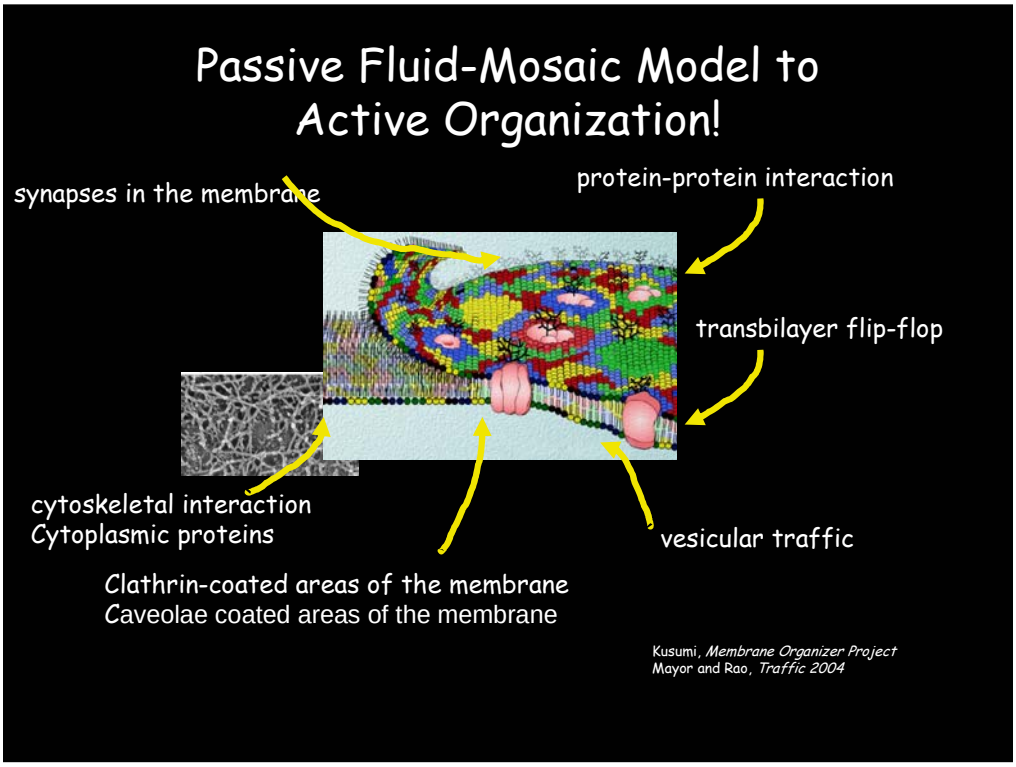
Membrane Skeleton Fence

EM analysis reveals actin substructure



Morone et al. JCB 2006


Active membranes domains: a working hypothesis
Images from Mayor/ Kusumi/Edidin/Borisy


Passive Fluid-Mosaic Model to
Active Organization!
synapses in the membrane
protein-protein interaction
transbilayer flip-flop
cytoskeletal interaction
Cytoplasmic proteins
vesicular traffic
Clathrin-coated areas of the membrane
Caveolae coated areas of the membrane
Kusumi, Membrane Organizer Project
Mayor and Rao, Traffic 2004