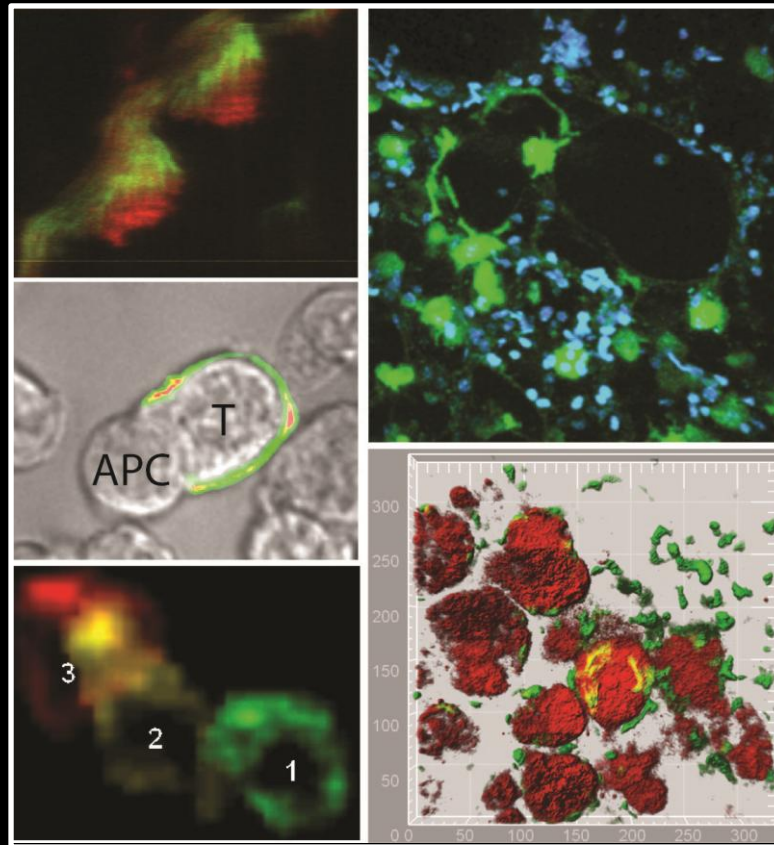
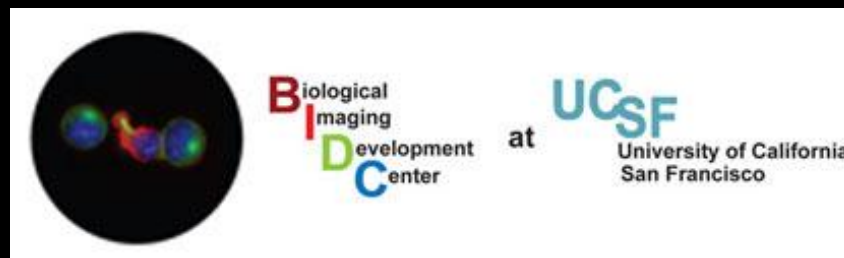


The Immune Bee-Hive: Motility, Interaction, and Collective Behavior.

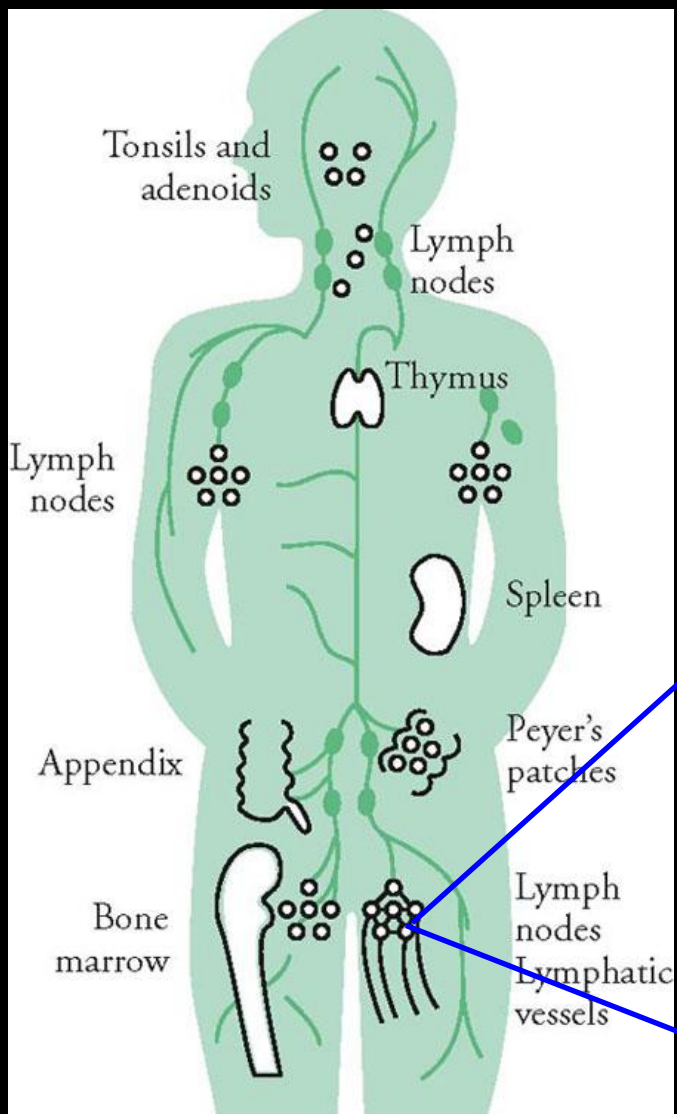


Krummel Lab, Department of Pathology



A Challenging Spatial Landscape for Communication/for Systemic Responses

[A complex community of T cells, B cells, NK, DC monocytes, Neutrophils, etc.]

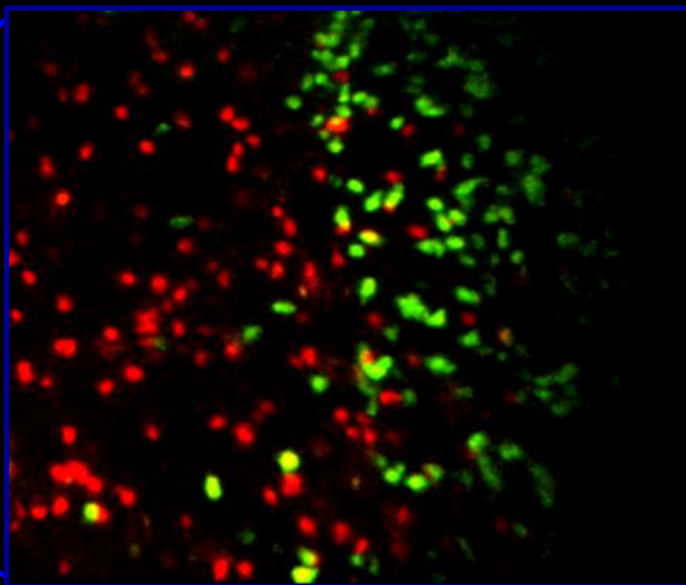


Lymphocyte Communication Does not Obey at least one Aristotelian Ideal: "Broadcast"

An entire city should be of a sufficiently small size that all citizens would be able to hear a single herald in peace or a single general in war [Politics VIII]

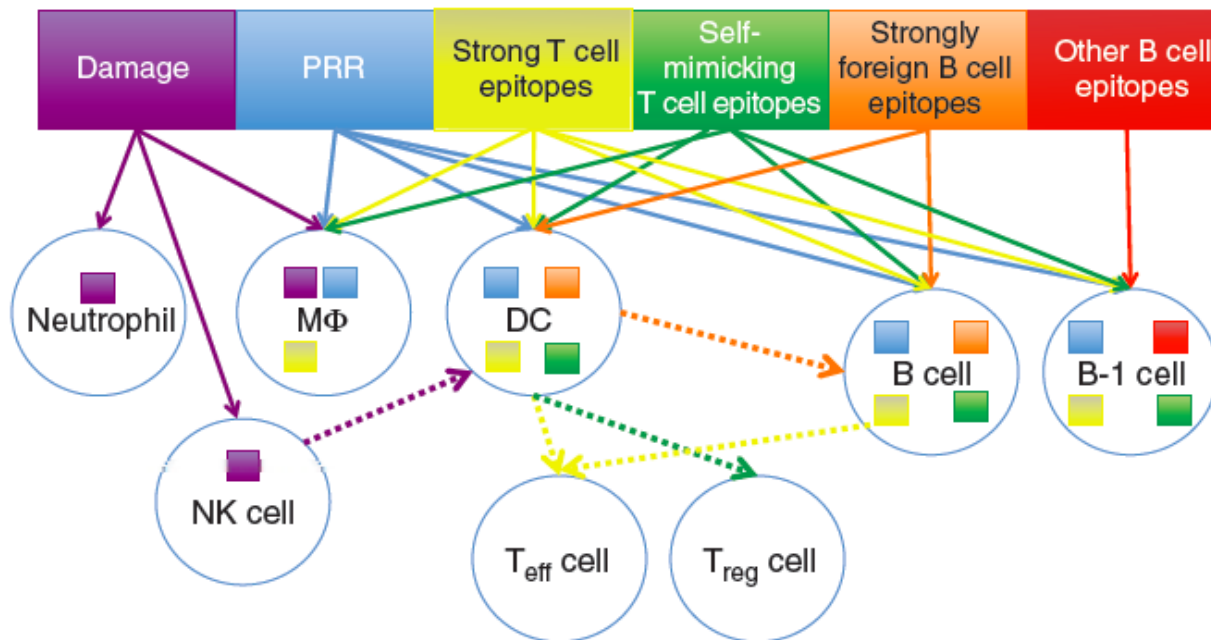
Rather, more akin to "Memetic".

Each Cell Acts to gather and disseminate information bits



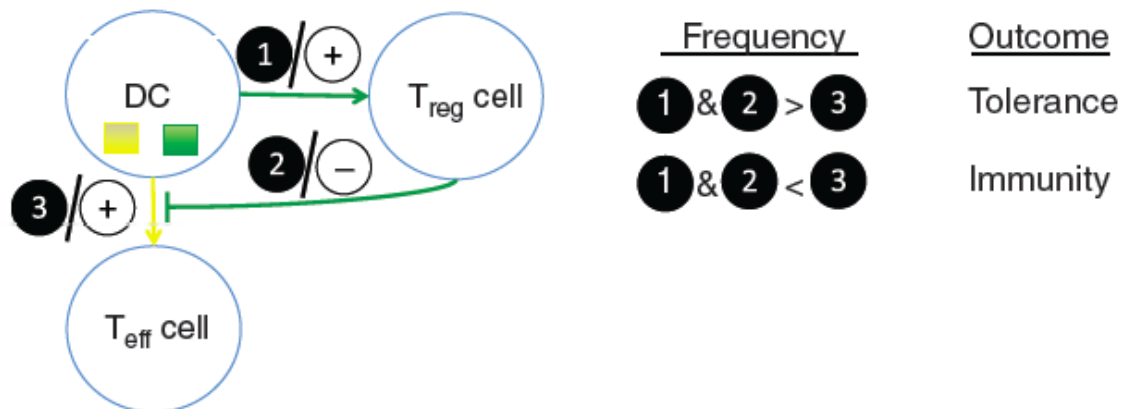
The Immune System as a Spatiotemporal Information System and a Spatial Coincidence Detector?

a



"The Insult"

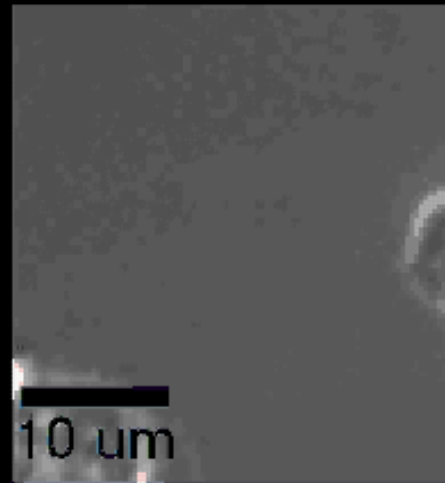
b



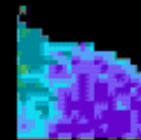
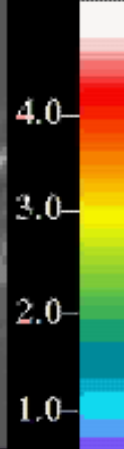
T cell Synapse Formation

CD3 ζ GFP Movement in Response to **TCR Agonist**

DIC



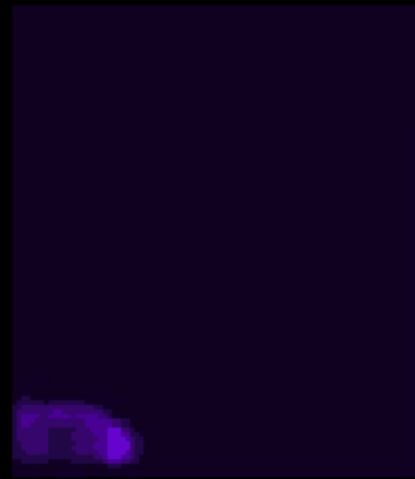
Fura Ratio:



Ca²⁺

GFP
Plane

Relative Intensity:



GFP
en face

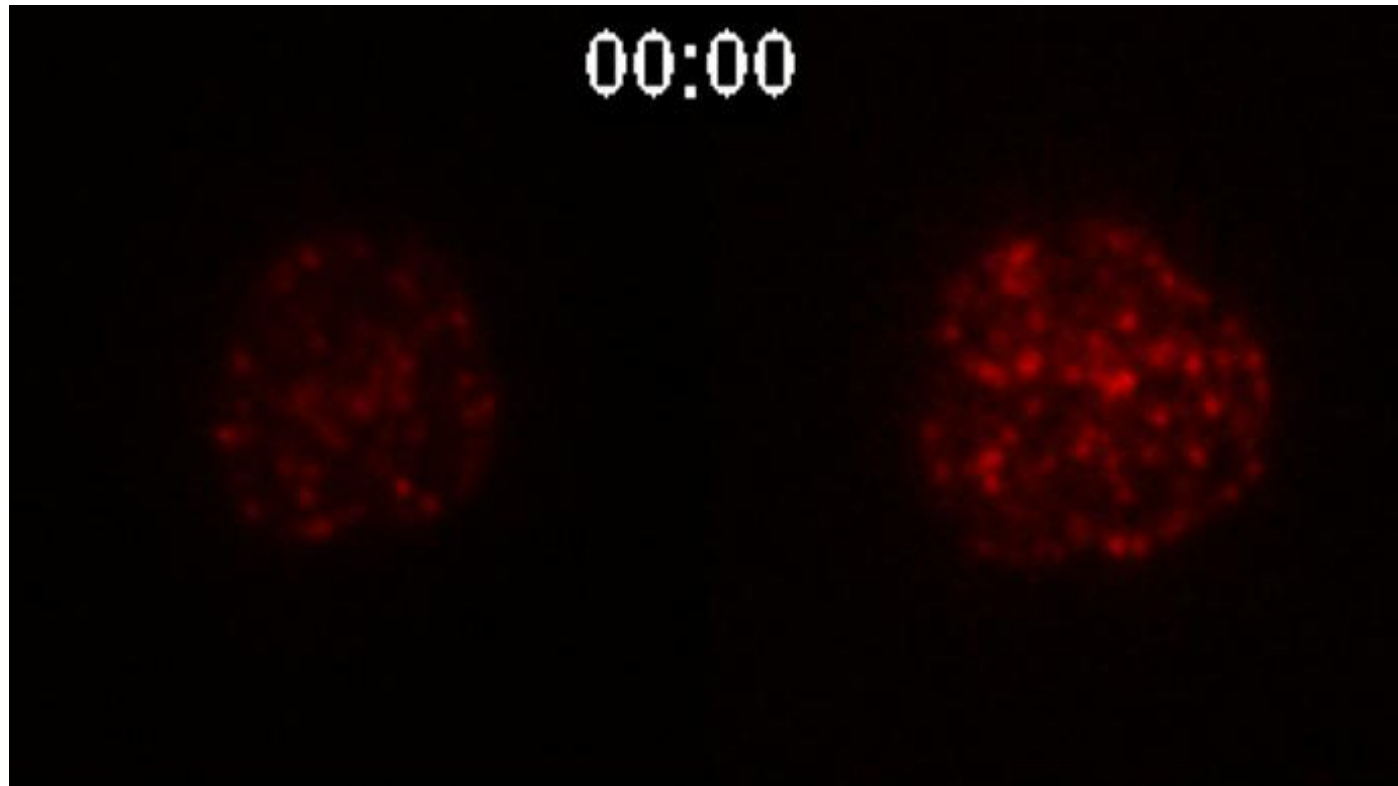
'Paradigm' Analysis of TCR movements in non-motile IS

“central SMAC” Formation

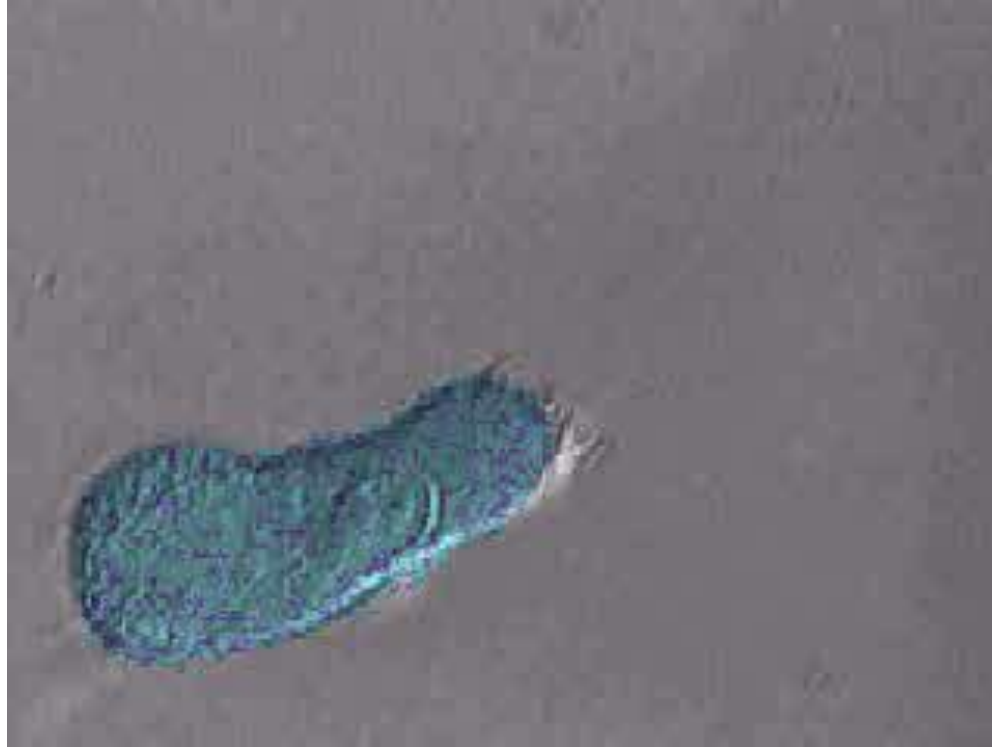
Imaged on lipid bilayers (pMHC/ICAM) through TIRF microscopy

OT-I

OT-I-GFP

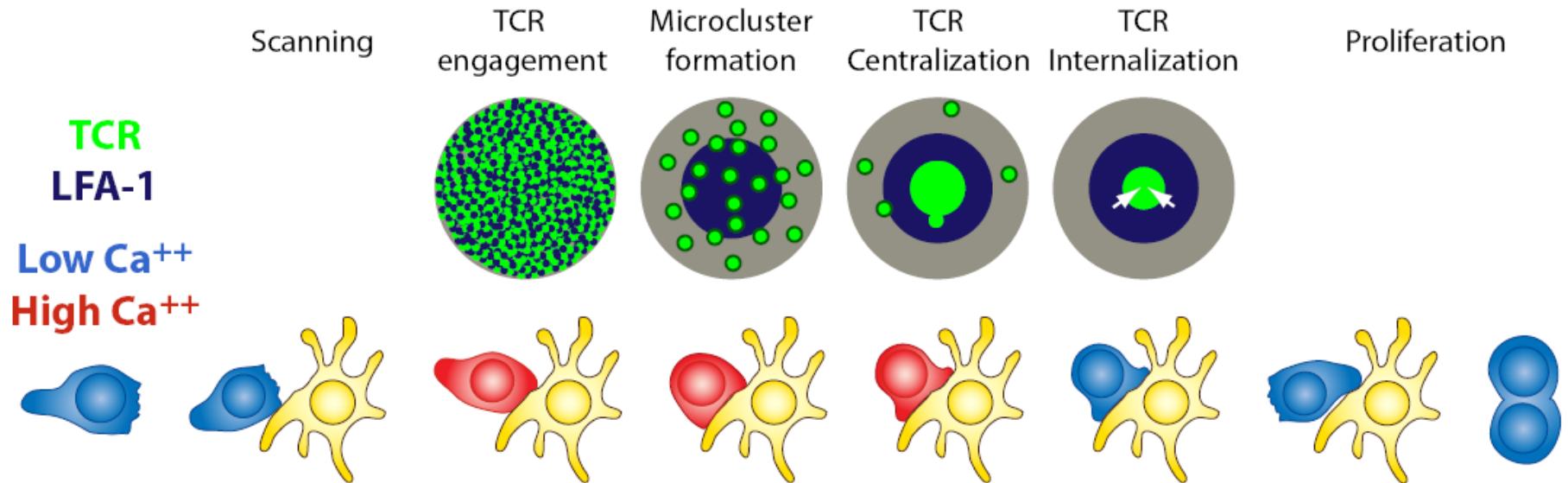


Stopping and Signaling ARE linked



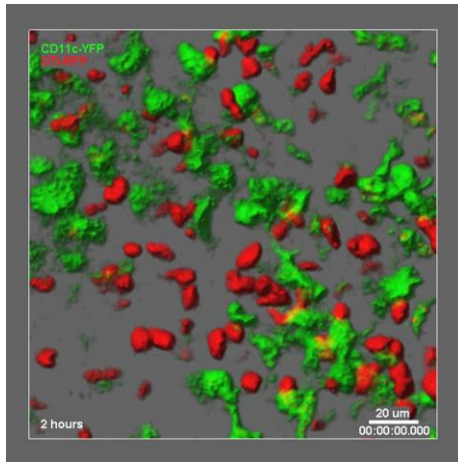
How does TCR Signaling/Clustering/Motility Take *Place in vivo*?

The immunological synapse paradigm

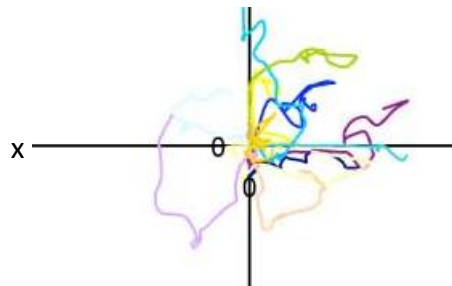


T-cell dynamics during the immune response

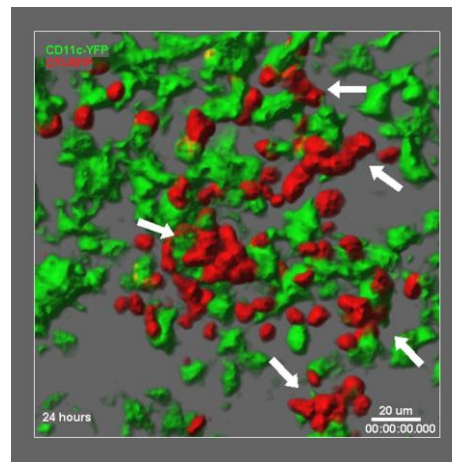
Phase 1: Transient contacts



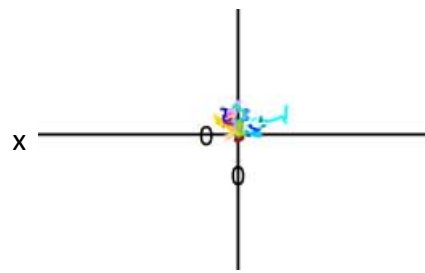
OTI T cells DCs



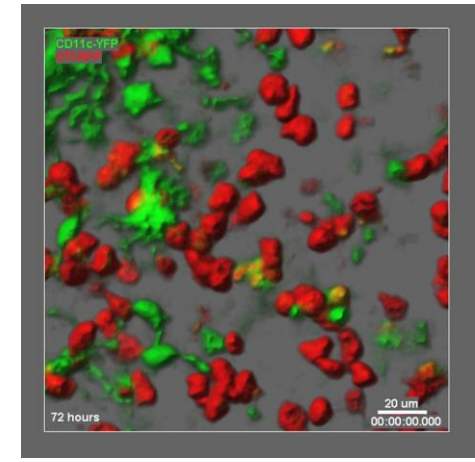
Phase 2: Arrest phase



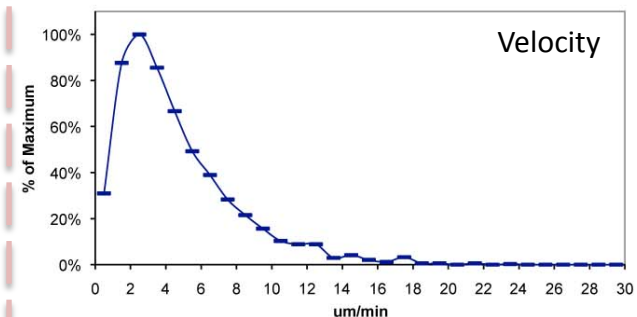
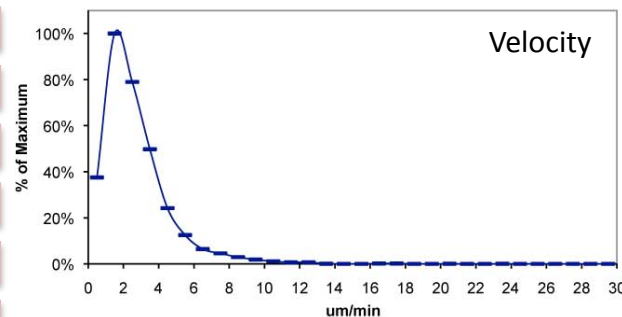
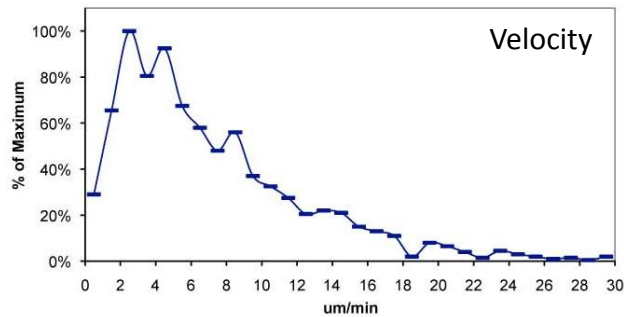
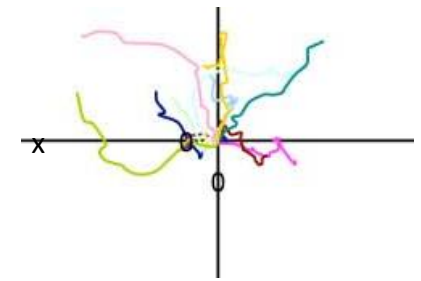
OTI T cells DCs



Phase 3: Swarming



OTI T cells DCs



DEC-OVA +
CD40 Ab

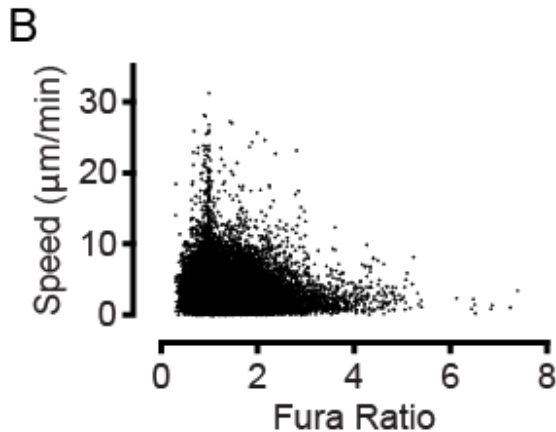
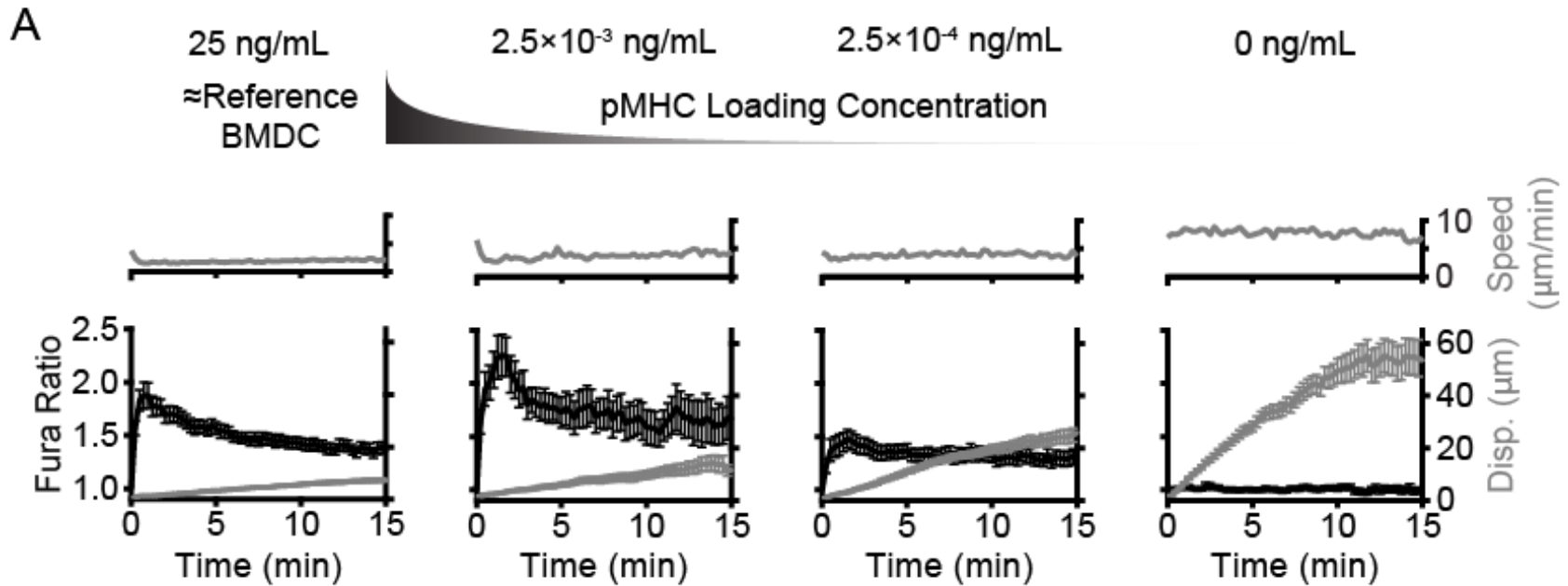
2h

24h

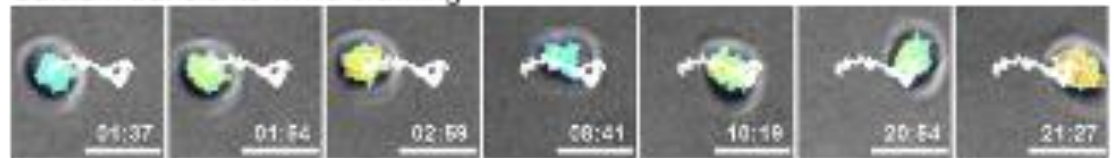
48h

Time

Motility and Signaling are Frequently co-incident:



e Calcium transients while crawling



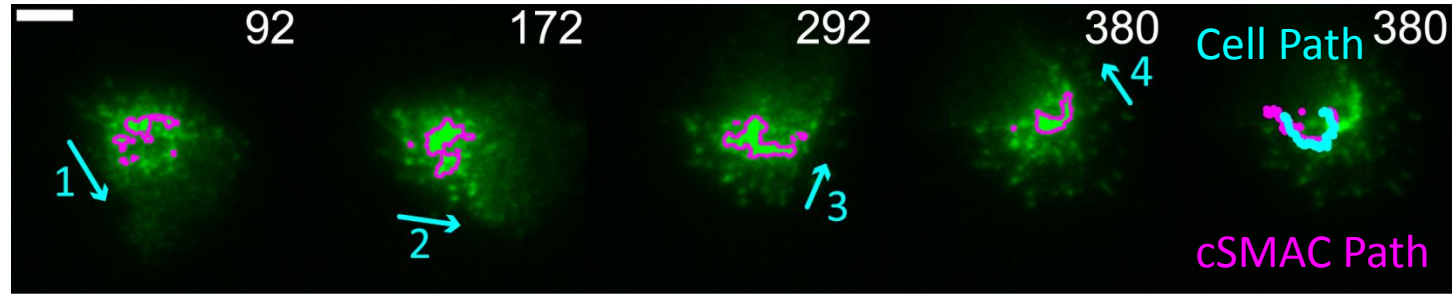
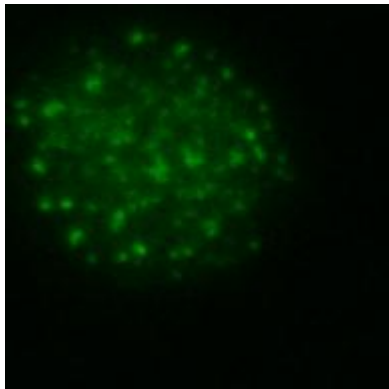
f Calcium signaling while arrested



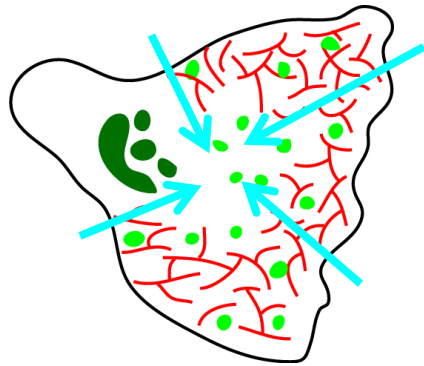
TCR Activation \rightarrow Ca^{2+} Flux

Does Not Obligate Cells to Arrest

Motile Synapses Reorganize 'On the Fly'

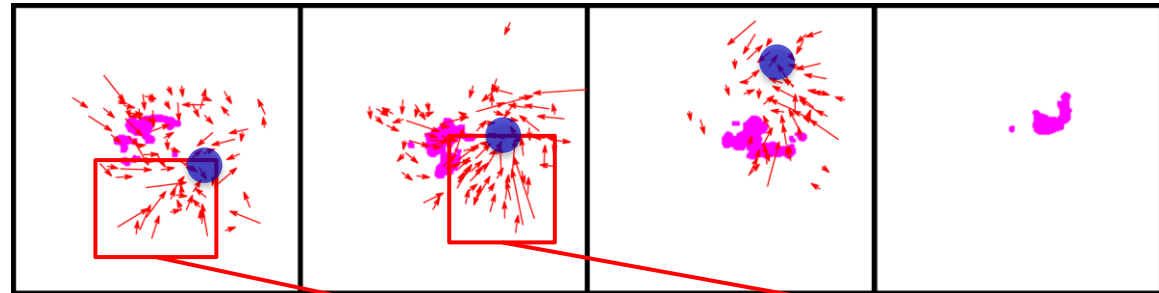


OT1 TCR microclusters changing direction with the cell
Microclusters move ahead of the cSMAC



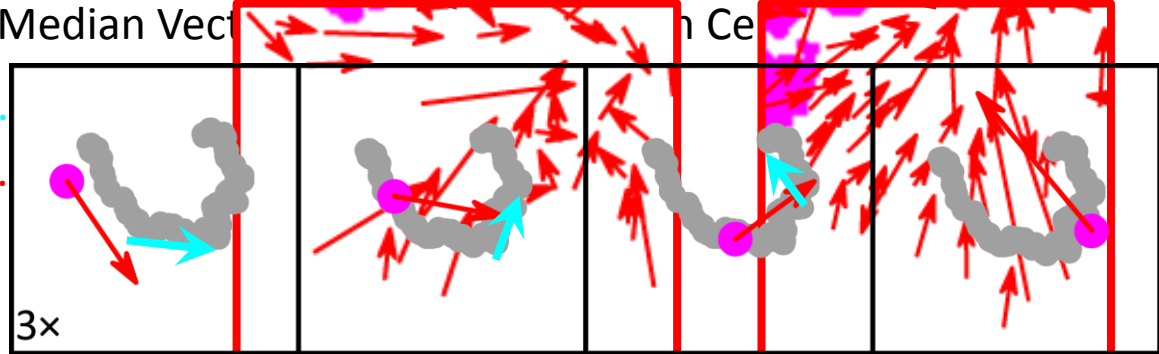
TCRs move toward an actin 'Void'

cSMAC
Microcluster Displacement



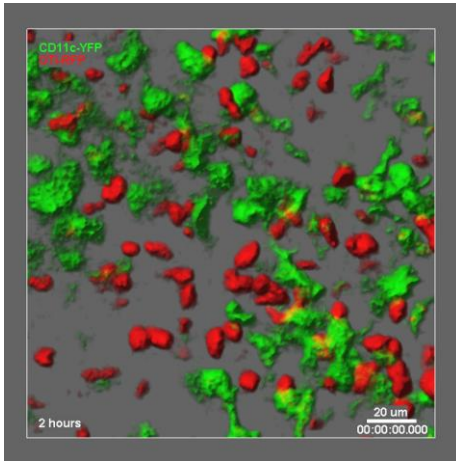
Median Vector

Cell Disp.
Microcluster Disp.
cSMAC
Cell Path
3x

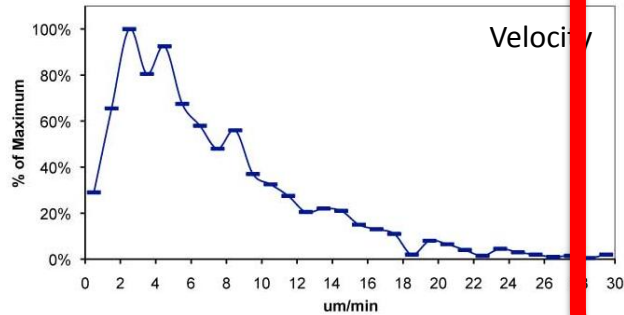
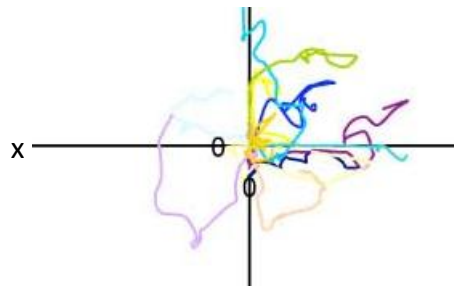


T-cell dynamics during the immune response

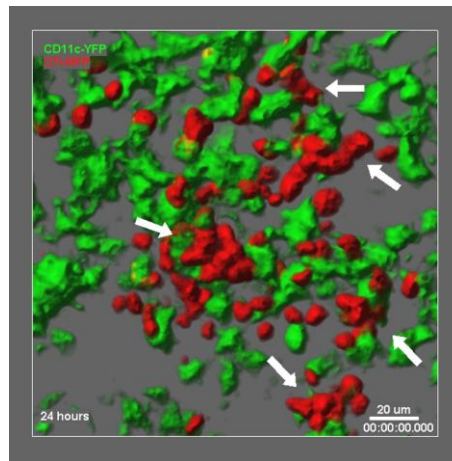
Phase 1: Transient contacts



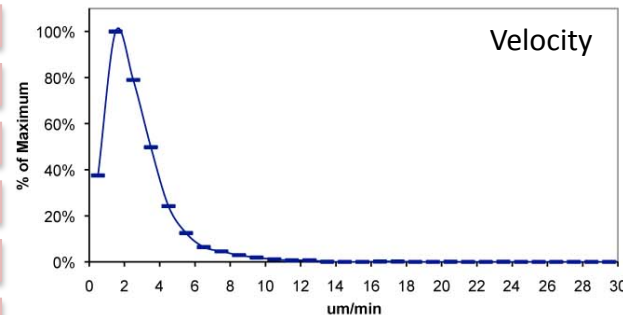
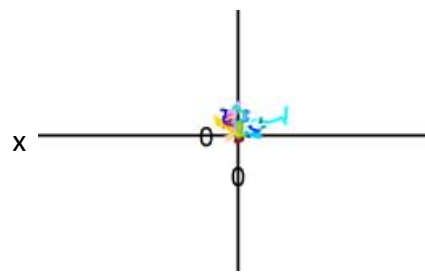
OTI T cells DCs



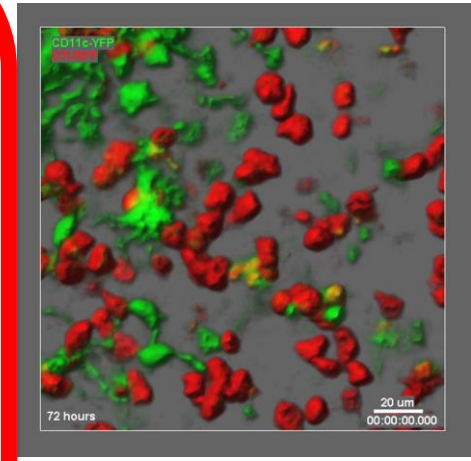
Phase 2: Arrest phase



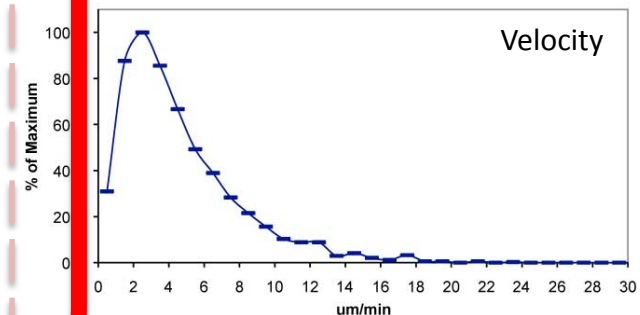
OTI T cells DCs



Phase 3: Swarming



OTI T cells DCs



DEC-OVA +
CD40 Ab

2h

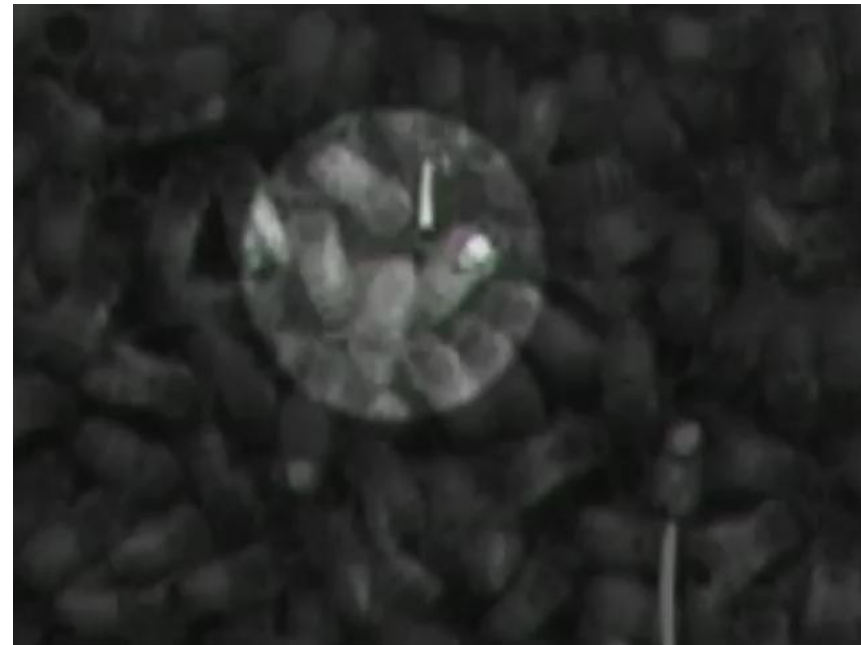
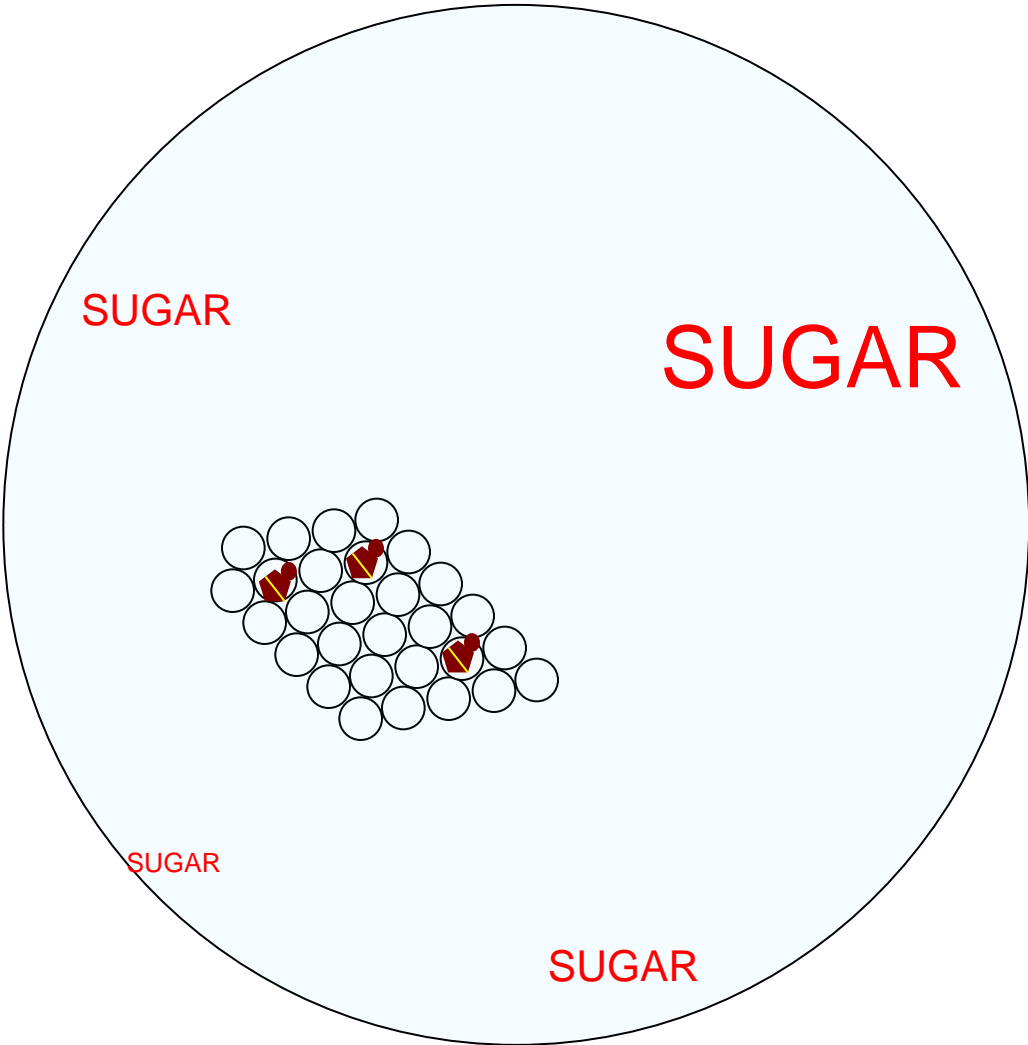
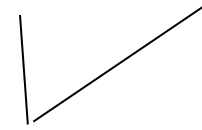
24h

48h

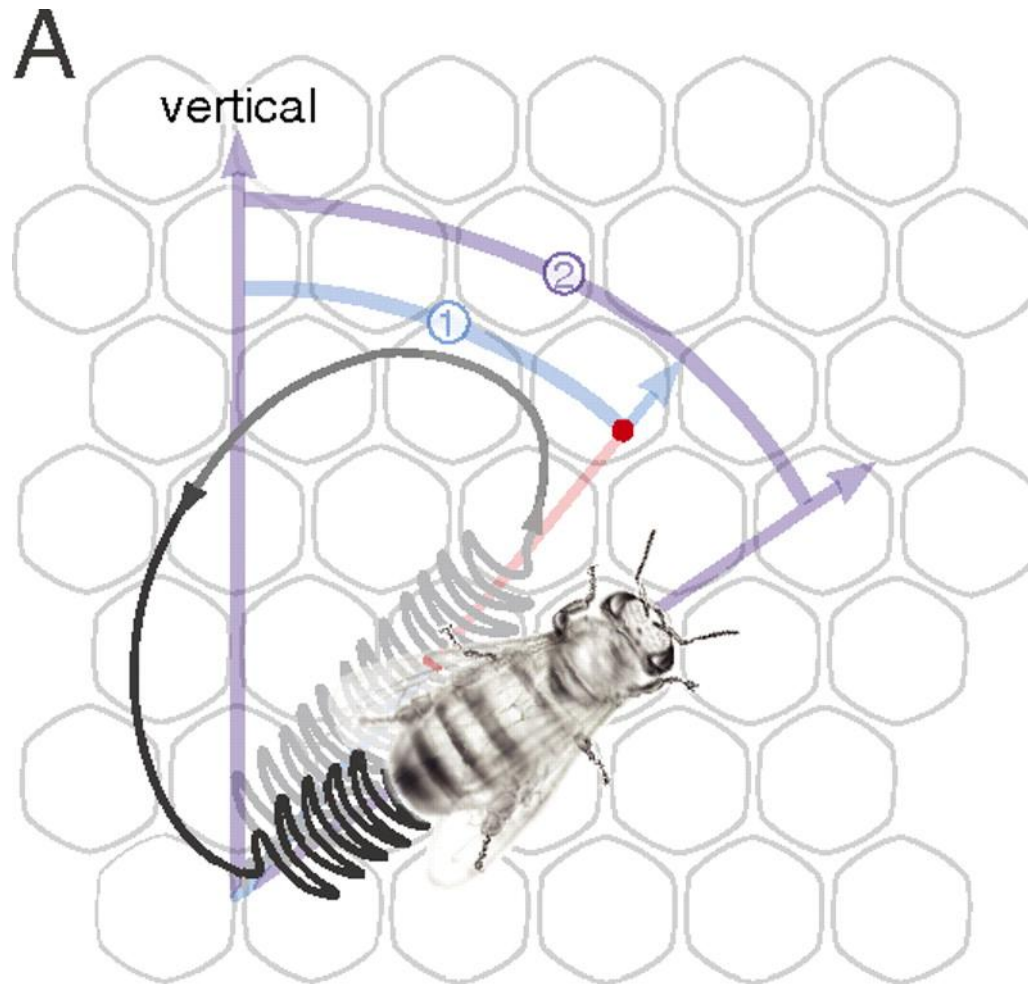
Time



Dancing Bees as Collectives

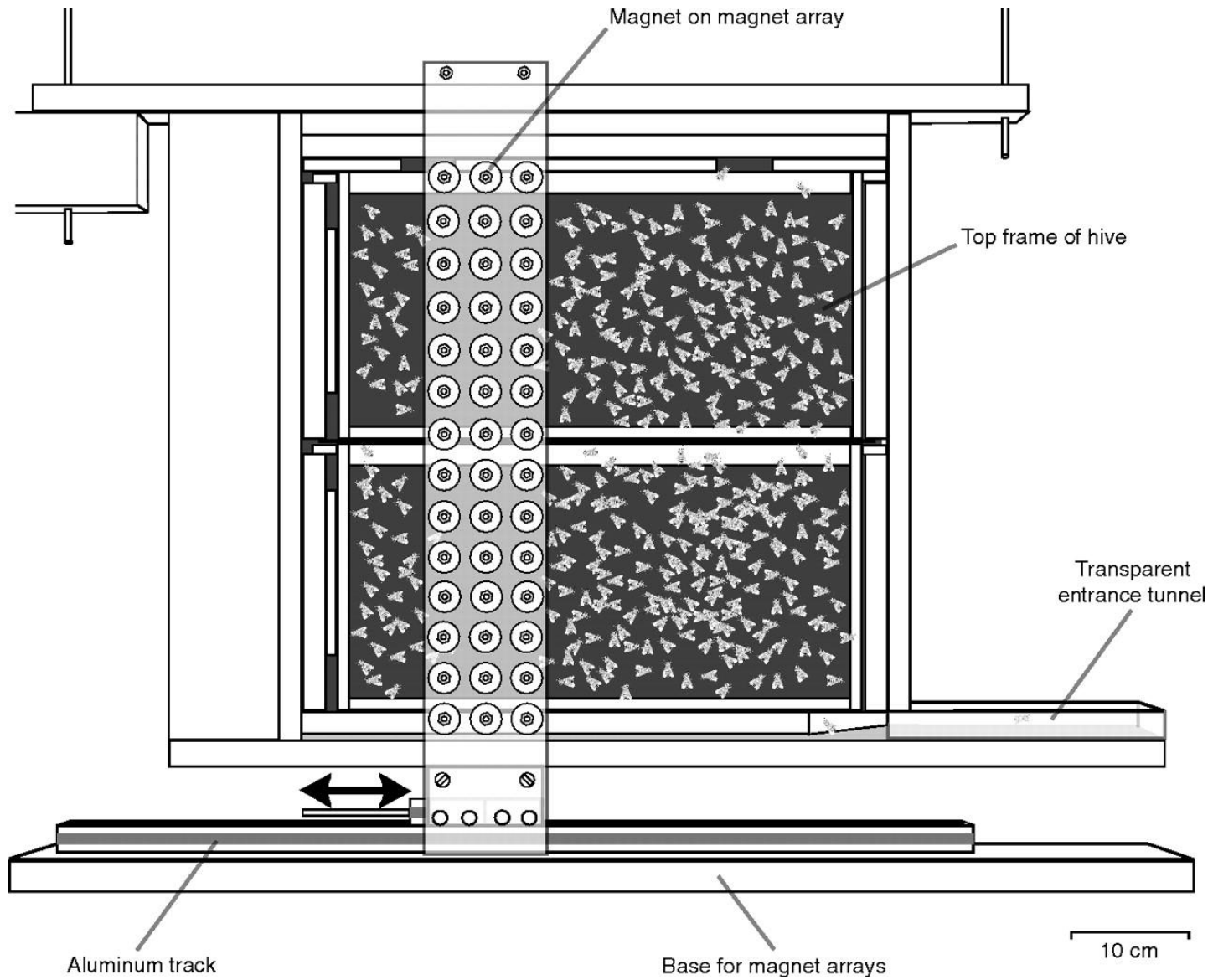


The dance move...



Klein B A et al. PNAS 2010;107:22705-22709

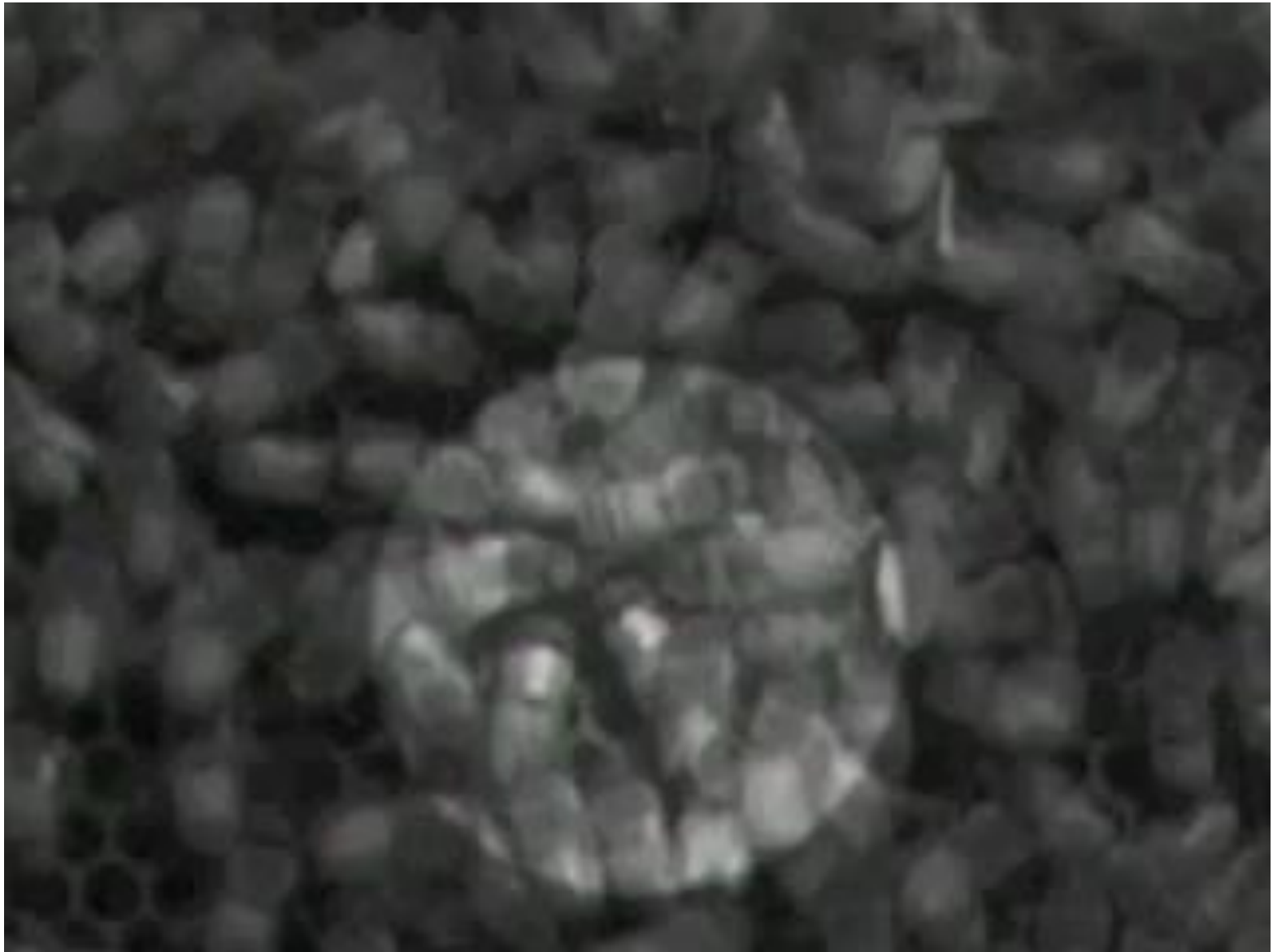
Anterior view of a two-frame observation hive and “insominator”.



Klein B A et al. PNAS 2010;107:22705-22709

PNAS

Sleep-Deprived Bees.



Klein B A et al. PNAS 2010;107:22705-22709

PNAS

What's the point of motility arrest redux



From Nature Reviews Immunology 8, 658-659 (September 2008)

A specialized T-T synapse

