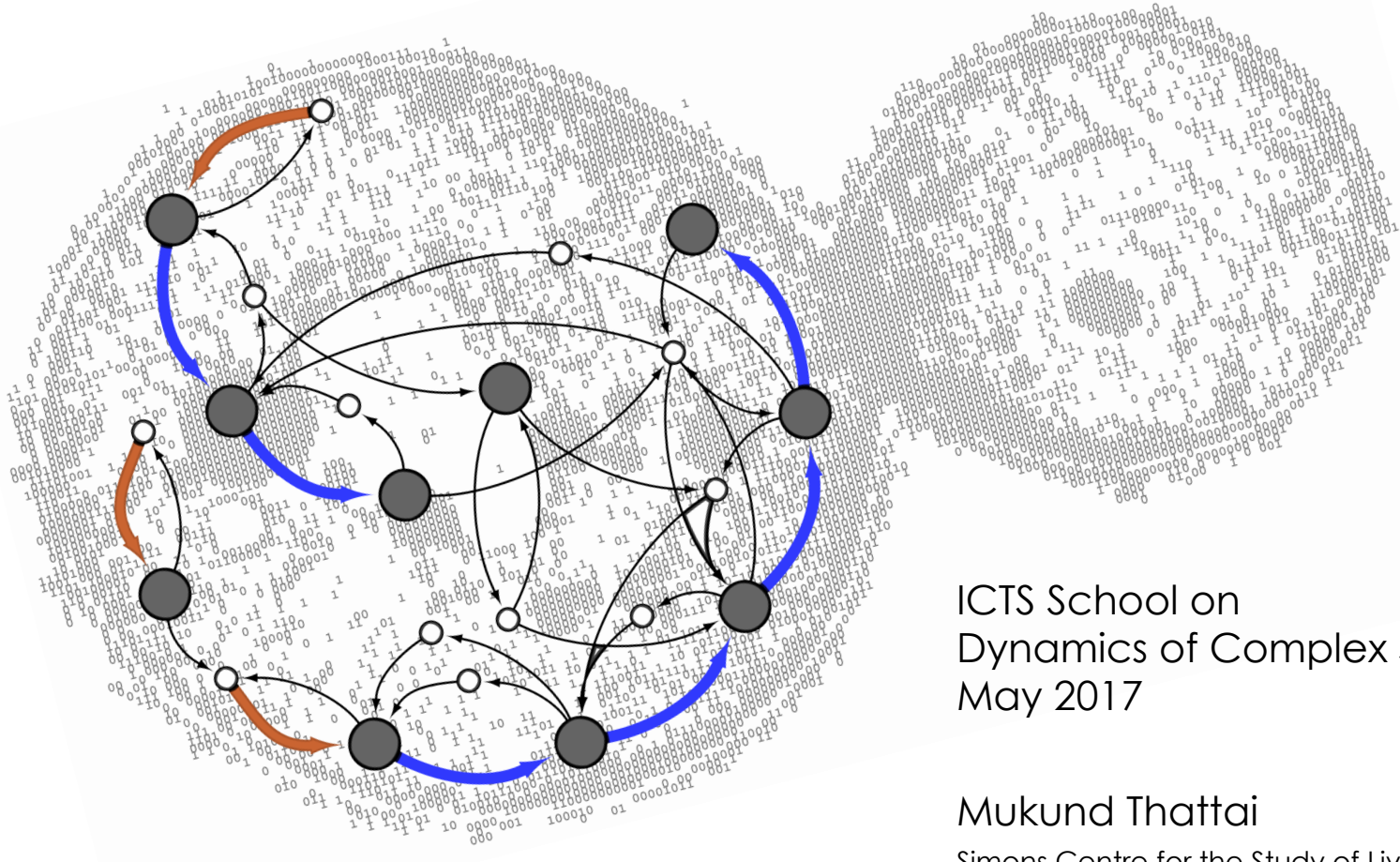
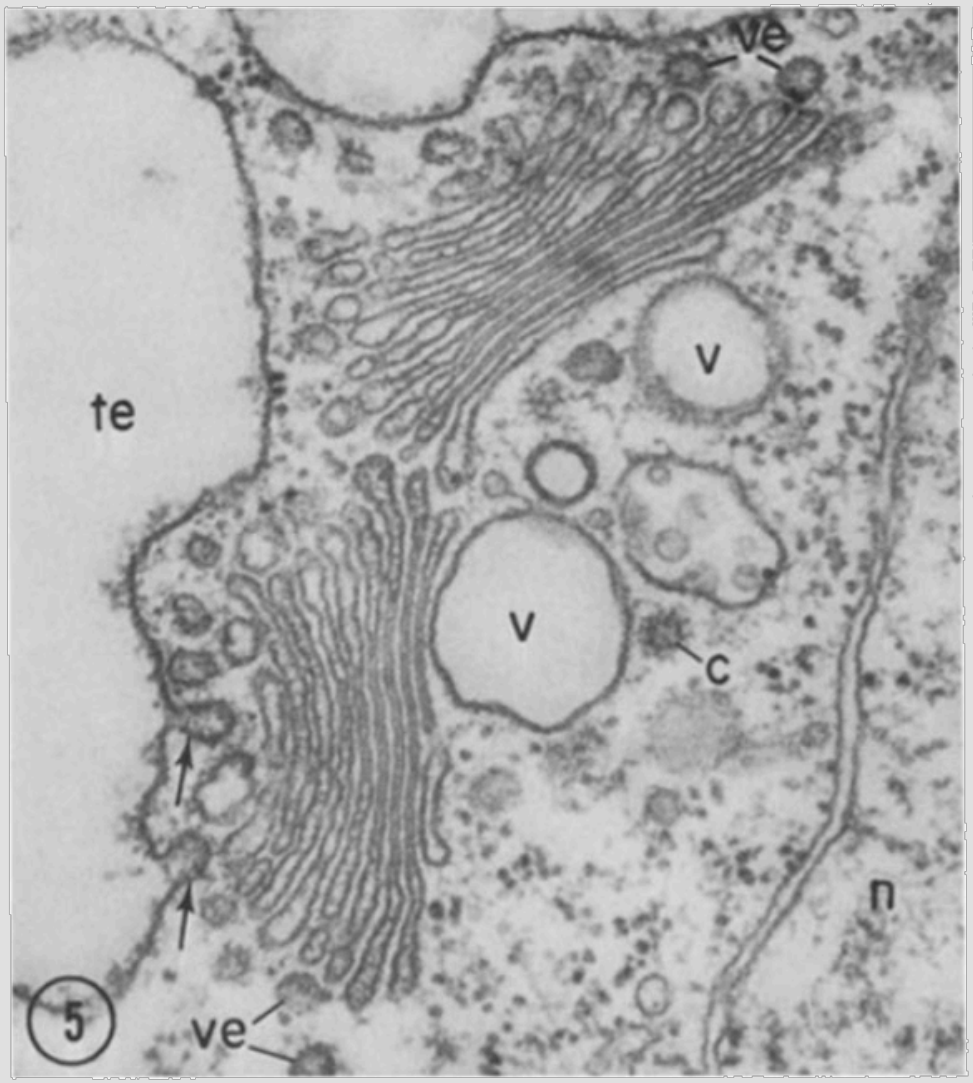
Dynamical models of membrane traffic: toward "statistical cell biology"

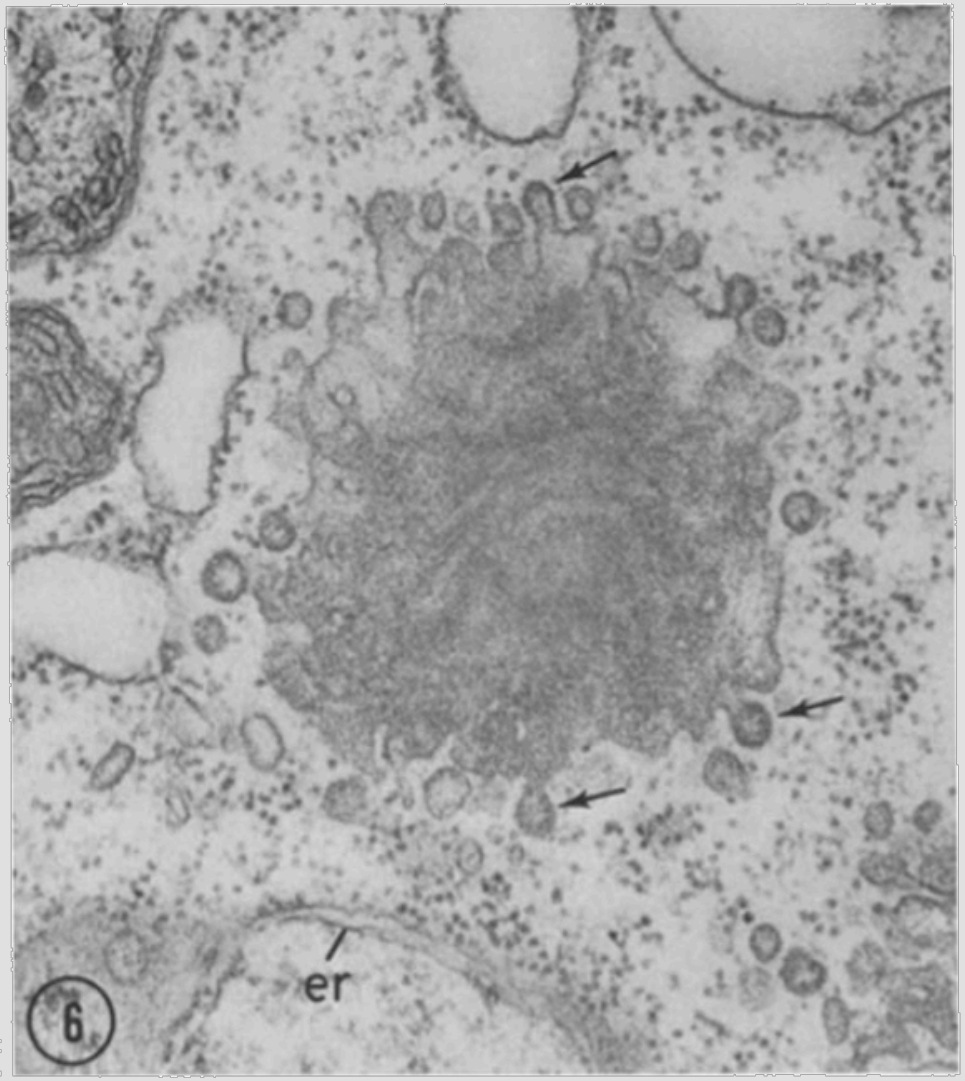


ICTS School on
Dynamics of Complex Systems
May 2017

Mukund Thattai
Simons Centre for the Study of Living Machines
National Centre for Biological Sciences
thattai@ncbs.res.in

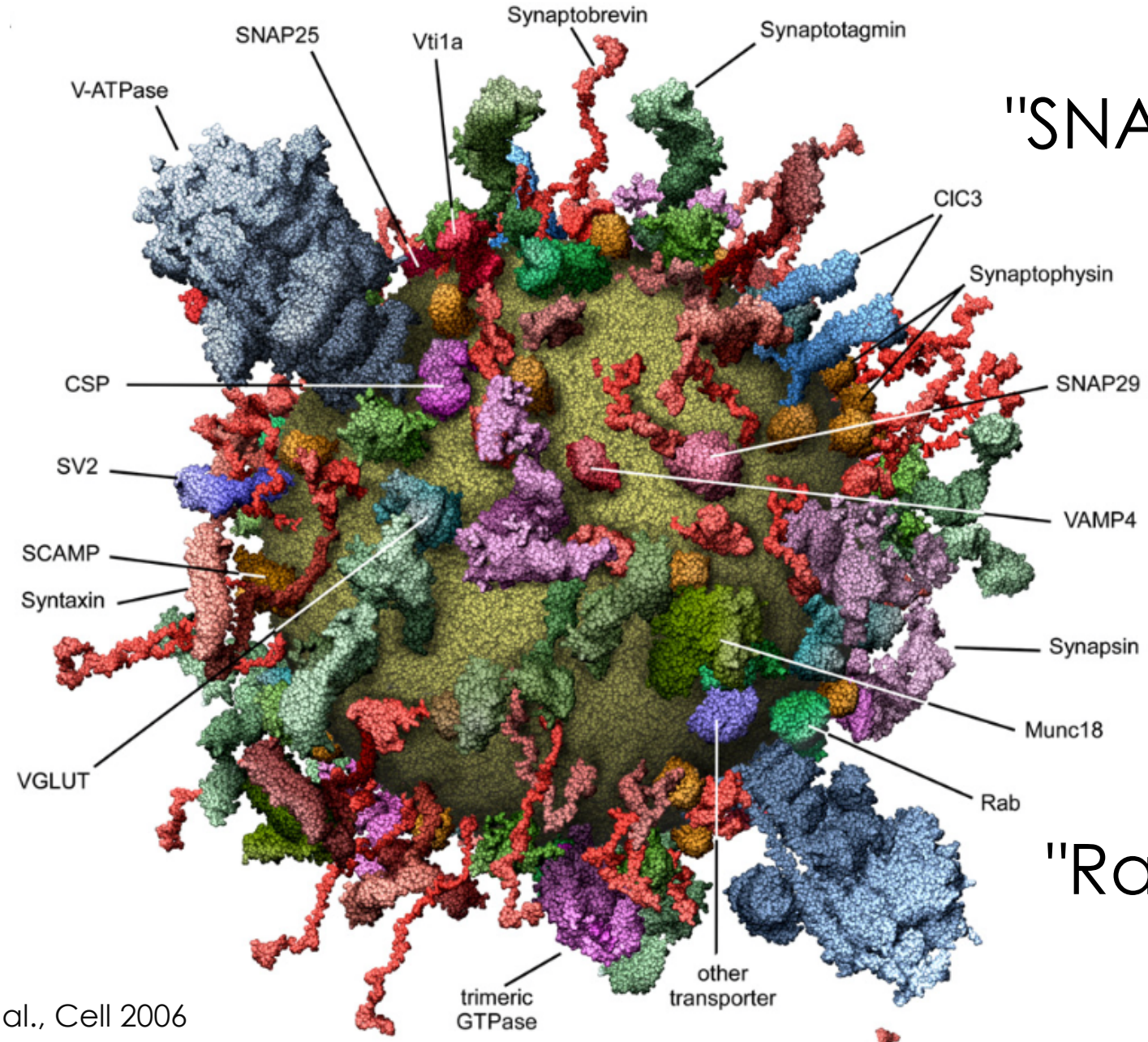
Ramya Purkanti





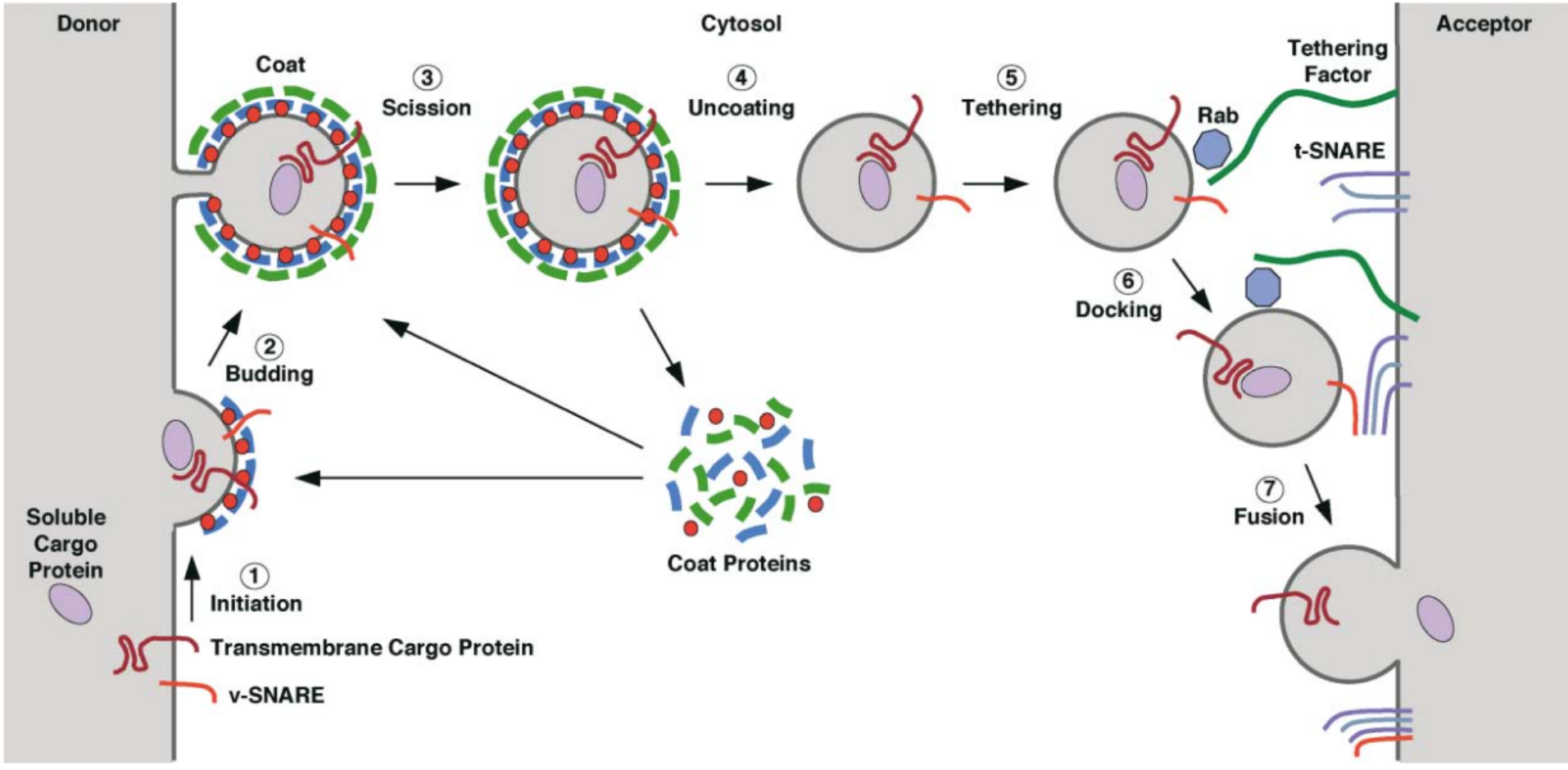
Farquhar & Palade, J Cell Biol 1981

A 40 nm transport vesicle



Takamori et al., Cell 2006

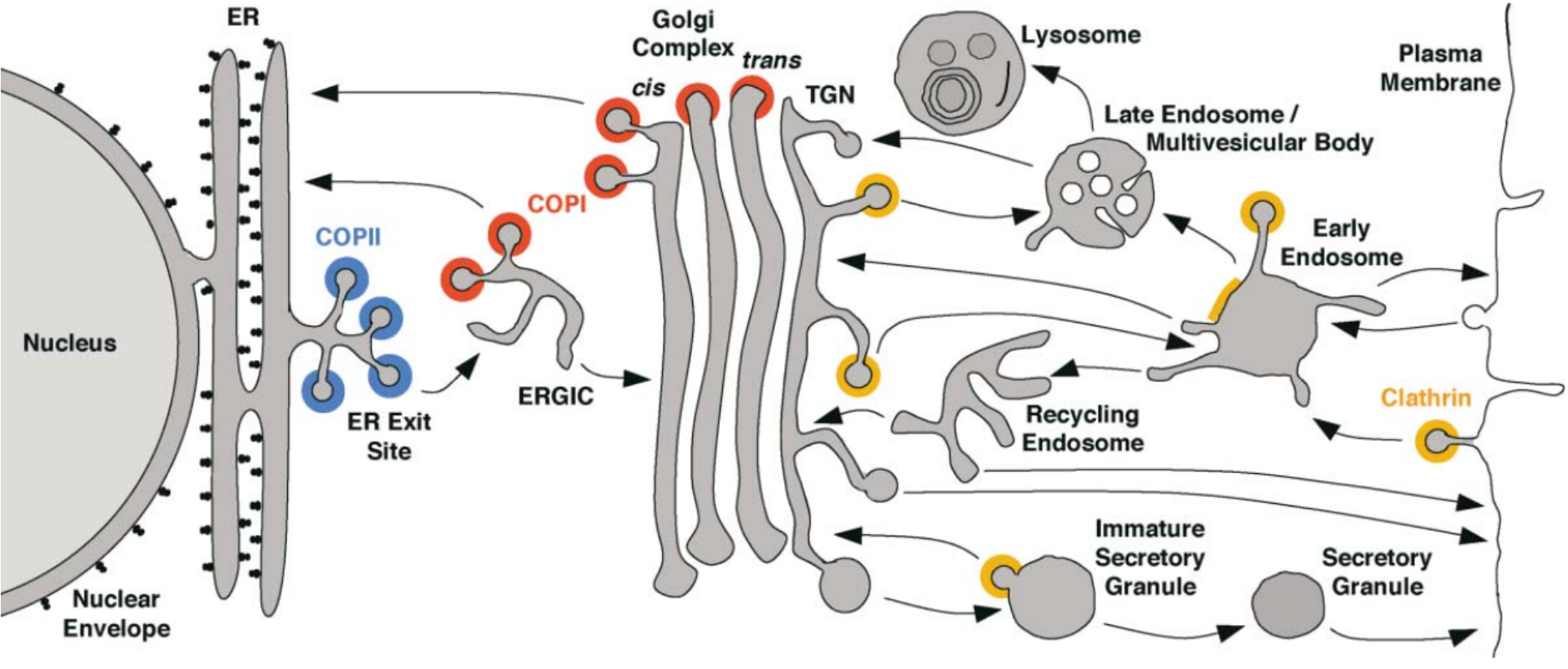
How do the transporters know where to go?



2013 Nobel Prize in Physiology or Medicine:
James E. Rothman, Randy W. Schekman, Thomas C. Südhof

Bonifacino & Glick, Cell 2004

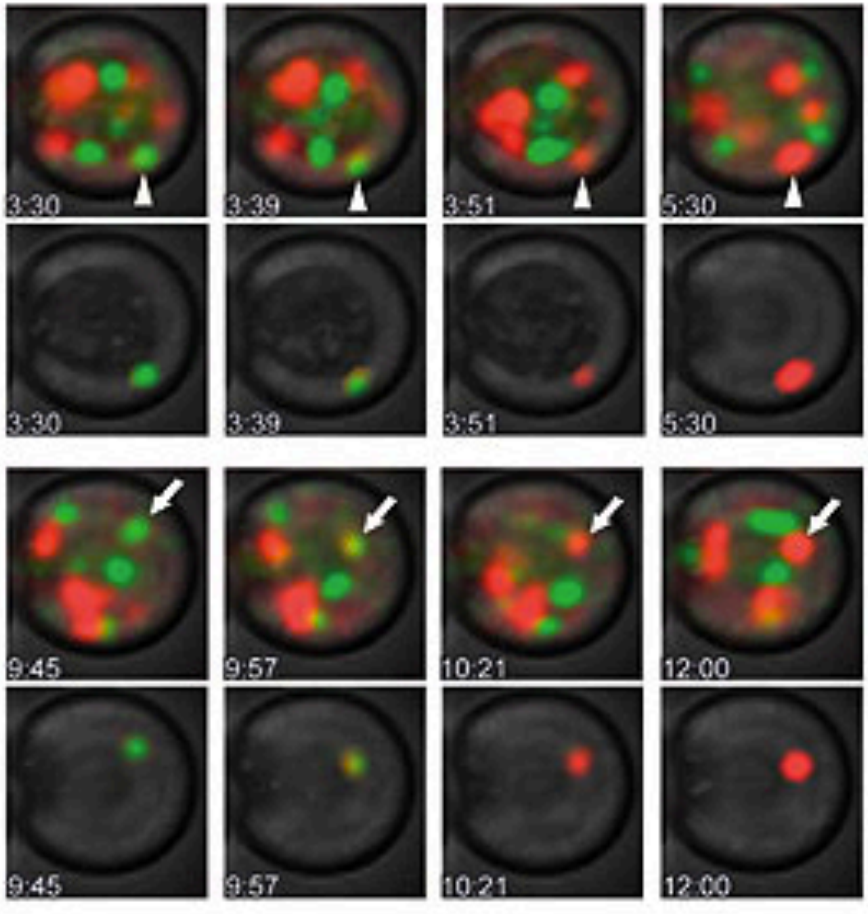
The dynamic membrane traffic system

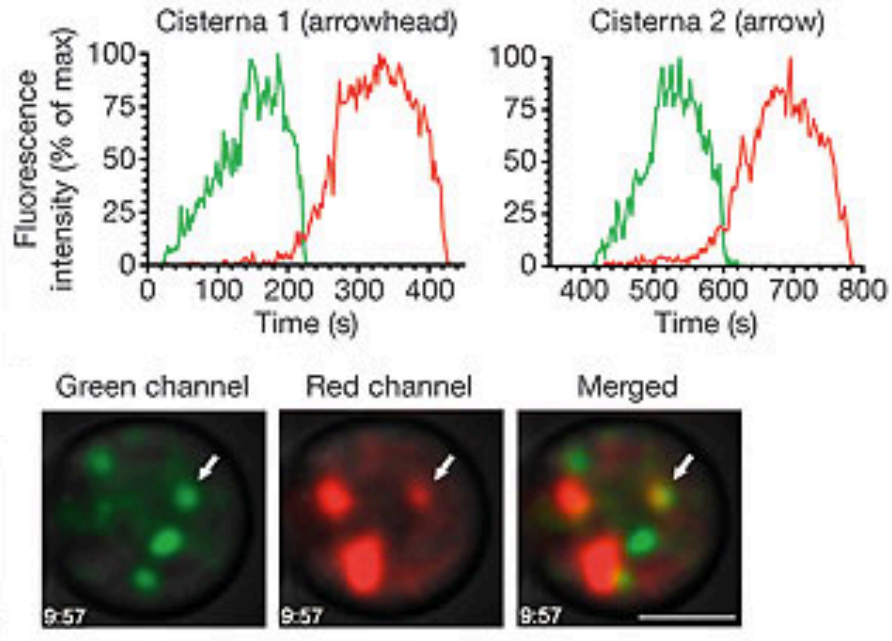


2013 Nobel Prize in Physiology or Medicine:
James E. Rothman, Randy W. Schekman, Thomas C. Südhof

Bonifacino & Glick, Cell 2004

Large cargo traverse the Golgi by "cisternal maturation"





Losev et al., Nature 2006

Modelling cisternal maturation

$$x_{tot} = \sum_{x,y} n(x,y)x,\ y_{tot} = \sum_{x,y} n(x,y)y$$

$$n_X \equiv n(1,0),\ n_Y \equiv n(0,1)$$

Stochastic description

Two X vesicles fuse homotypically to create a compartment :

$n_X \downarrow_2, n(2,0) \uparrow^1$ rate $An_X(n_X - 1)$

A compartment buds an X or Y vesicle :

$n_X \uparrow^1 n(x,y) \downarrow_1, n(x-1,y) \uparrow^1$ rate $Bx\, n(x,y)$

$n_Y \uparrow^1 n(x,y) \downarrow_1, n(x,y-1) \uparrow^1$ rate $Dy\, n(x,y)$

A compartment fuses to an X or Y vesicle :

$n_X \downarrow_1 n(x,y) \downarrow_1, n(x+1,y) \uparrow^1$ rate $A\frac{x^2}{(x+y)^2} n_X n(x,y)$

$n_Y \downarrow_1 n(x,y) \downarrow_1, n(x,y+1) \uparrow^1$ rate $Cx\, n_Y n(x,y)$

Deterministic description

$$\frac{dx}{dt} = A\overline{n_X}\frac{x^2}{(x+y)^2} - Bx$$

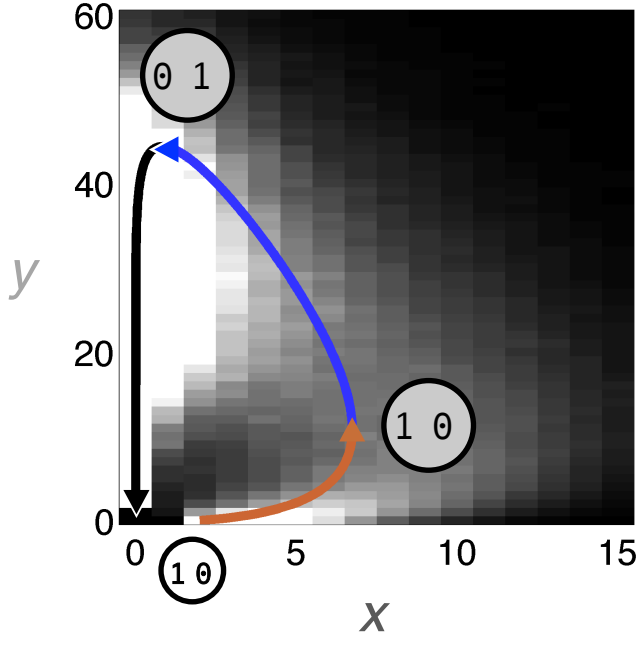
$$\frac{dy}{dt} = C\overline{n_Y}x - Dy$$

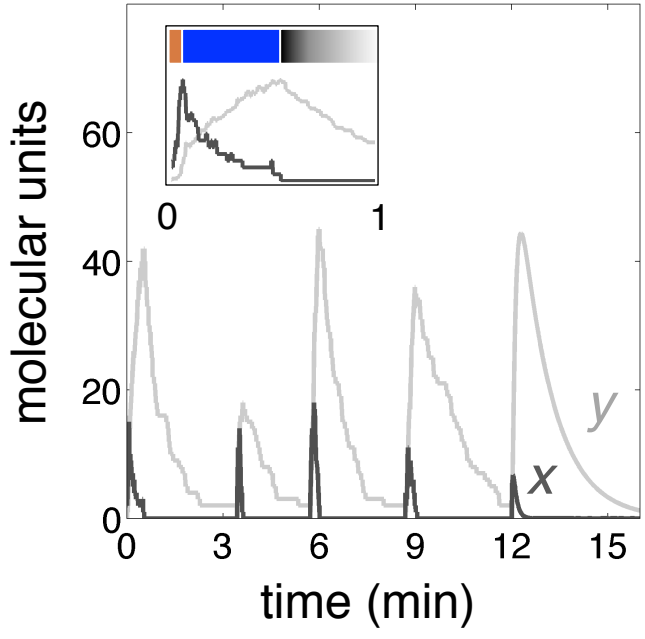
Hopf bifurcation

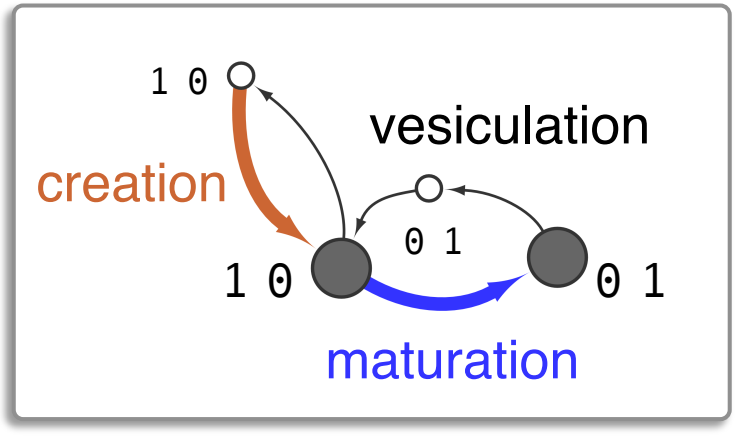
$$\frac{B}{B+D}\,\frac{C\overline{n_Y}}{C\overline{n_Y}+D} > \frac{1}{2}$$

Mani & Thattai, eLife 2016

Modelling cisternal maturation

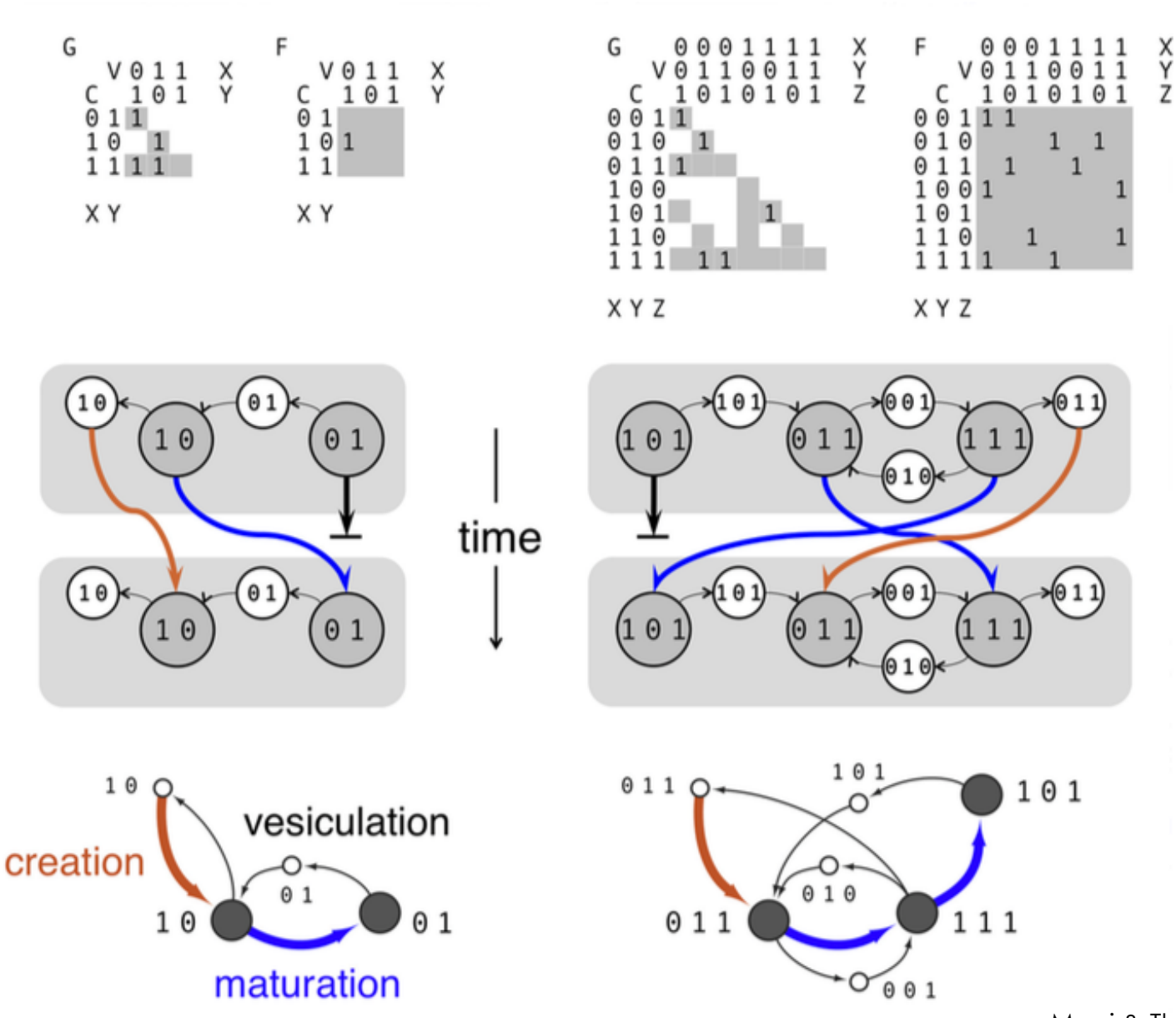




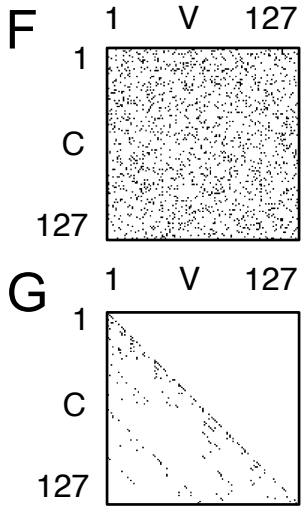


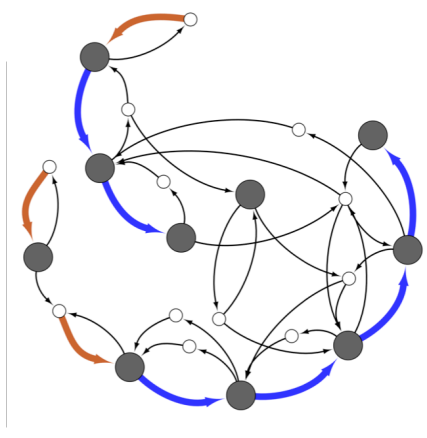
Mani & Thattai, eLife 2016

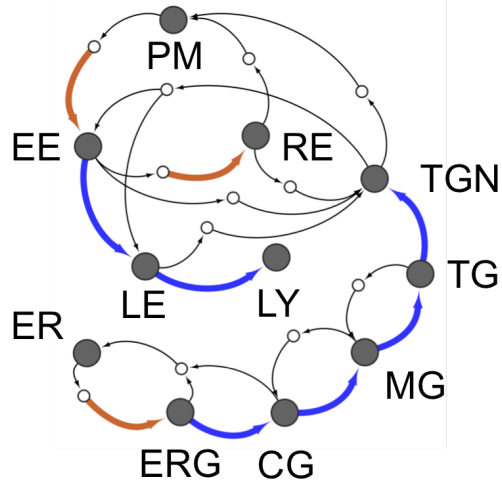
A Boolean model of vesicle traffic

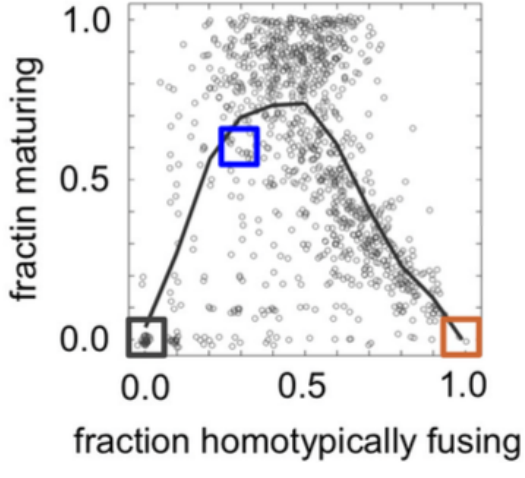


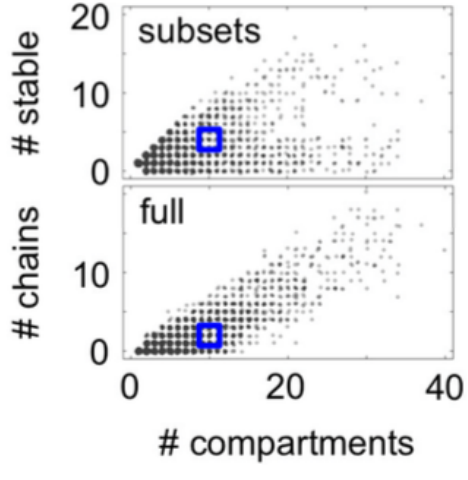
Random budding and fusion rules generate cell-like networks





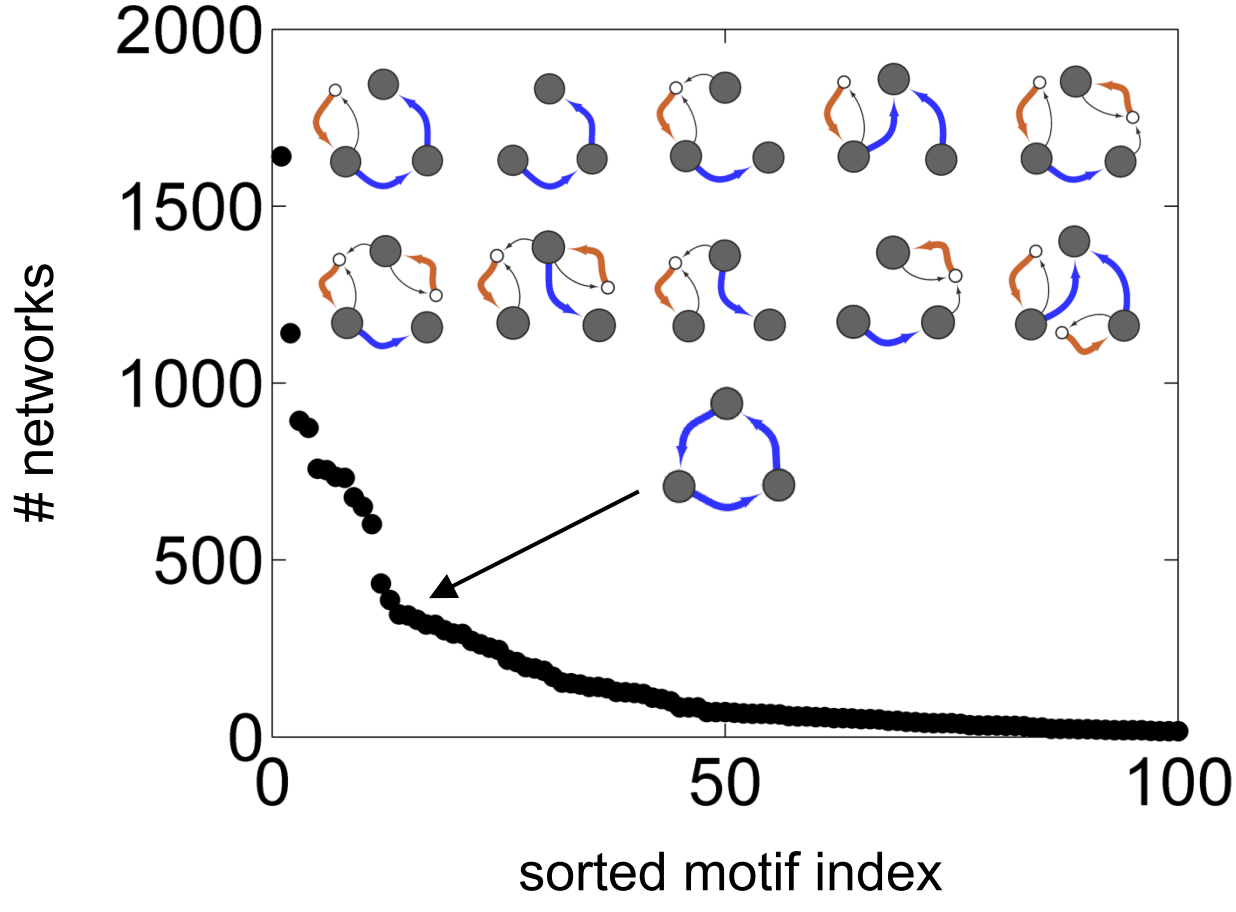






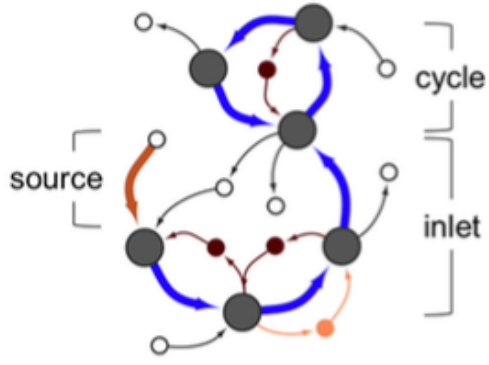
Mani & Thattai, eLife 2016

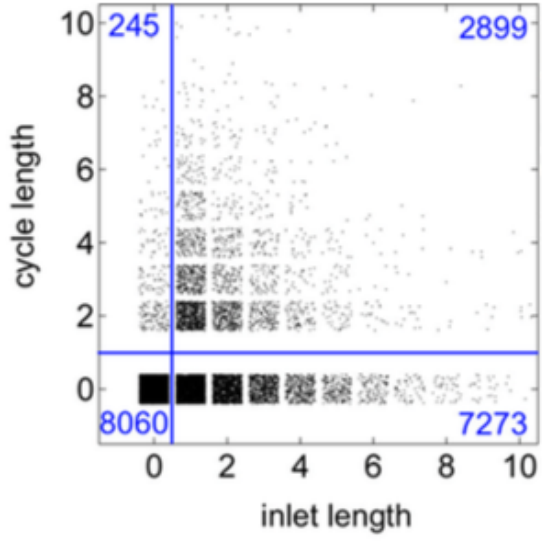
Enriched motifs in vesicle traffic networks with random budding and fusion rules

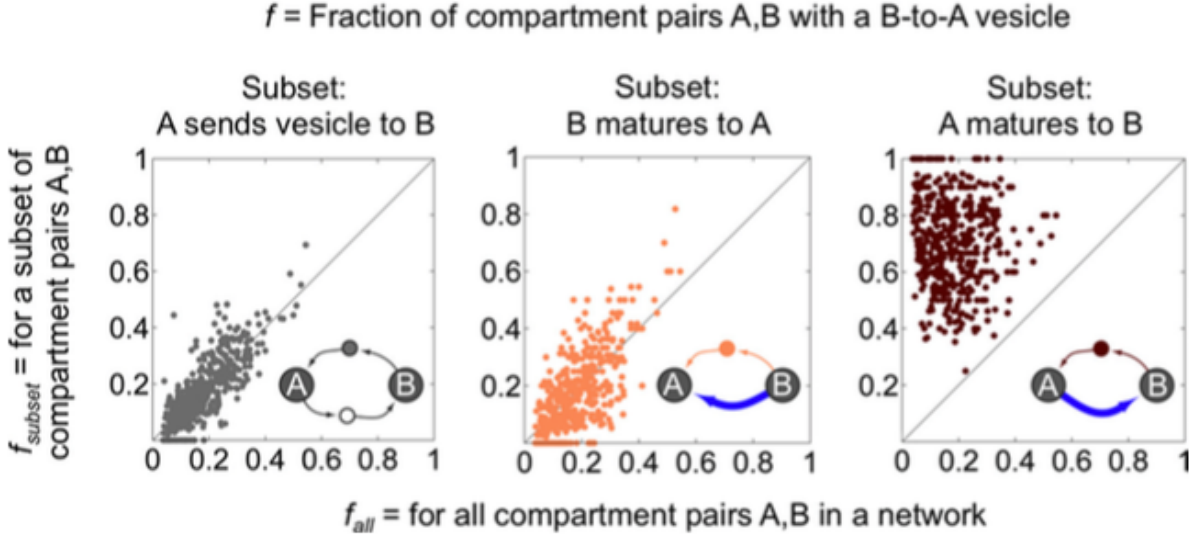


Mani & Thattai, eLife 2016

The "maturation chain" motif

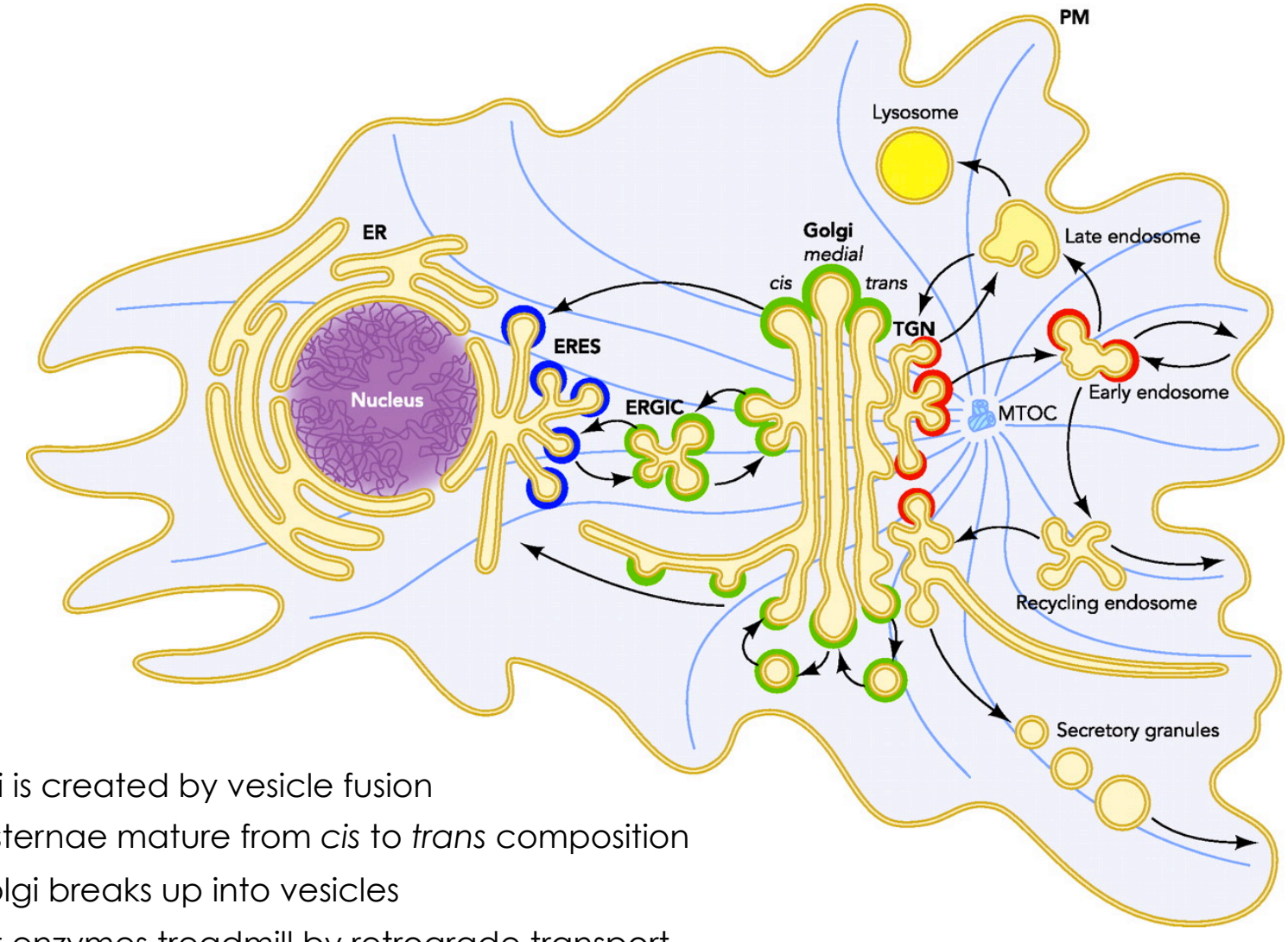






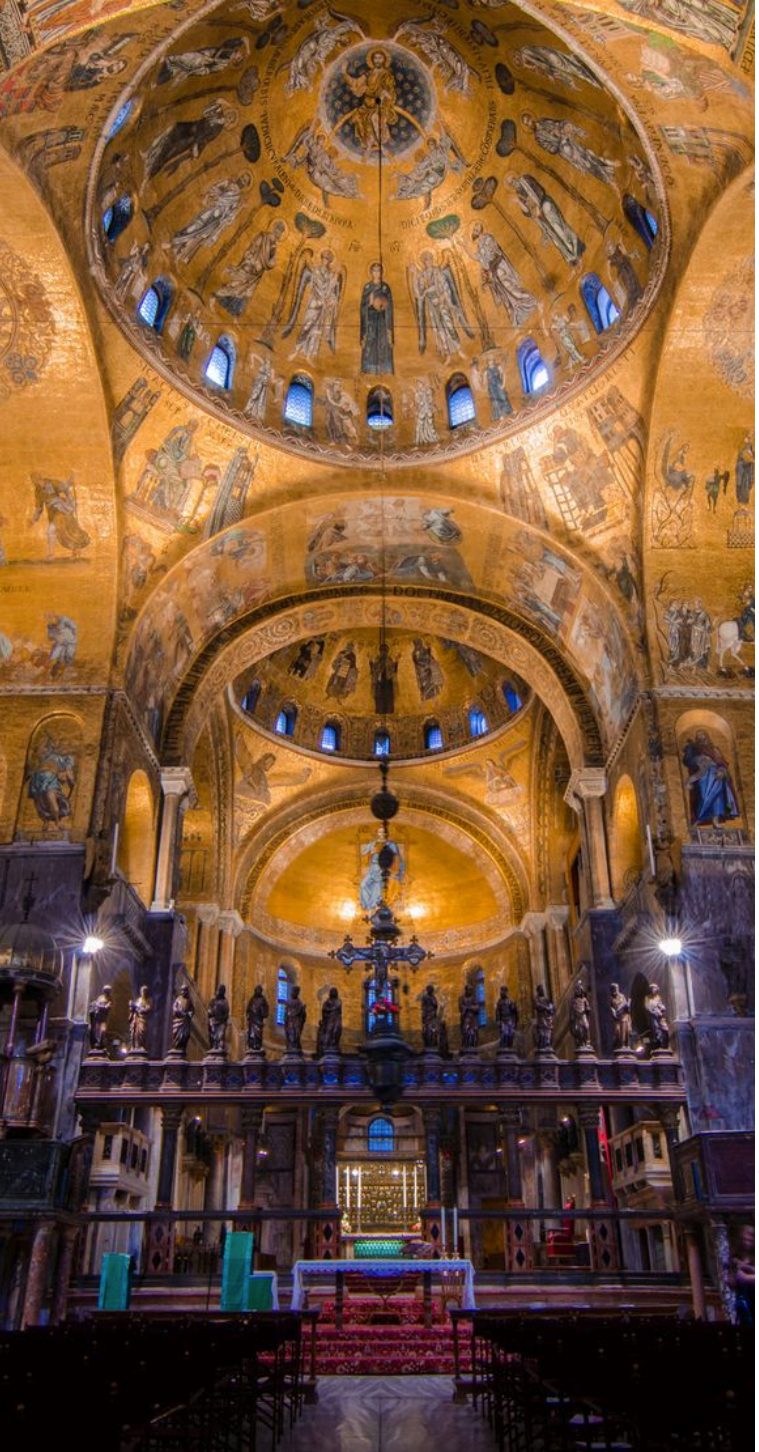
Mani & Thattai, eLife 2016

Retrograde vesicles drive maturation in real cells!



1. *cis*-Golgi is created by vesicle fusion
2. Golgi cisternae mature from *cis* to *trans* composition
3. *trans*-Golgi breaks up into vesicles
4. Resident enzymes treadmill by retrograde transport
5. In some species the Golgi has a stacked morphology

Szul & Sztul, Physiology 2011



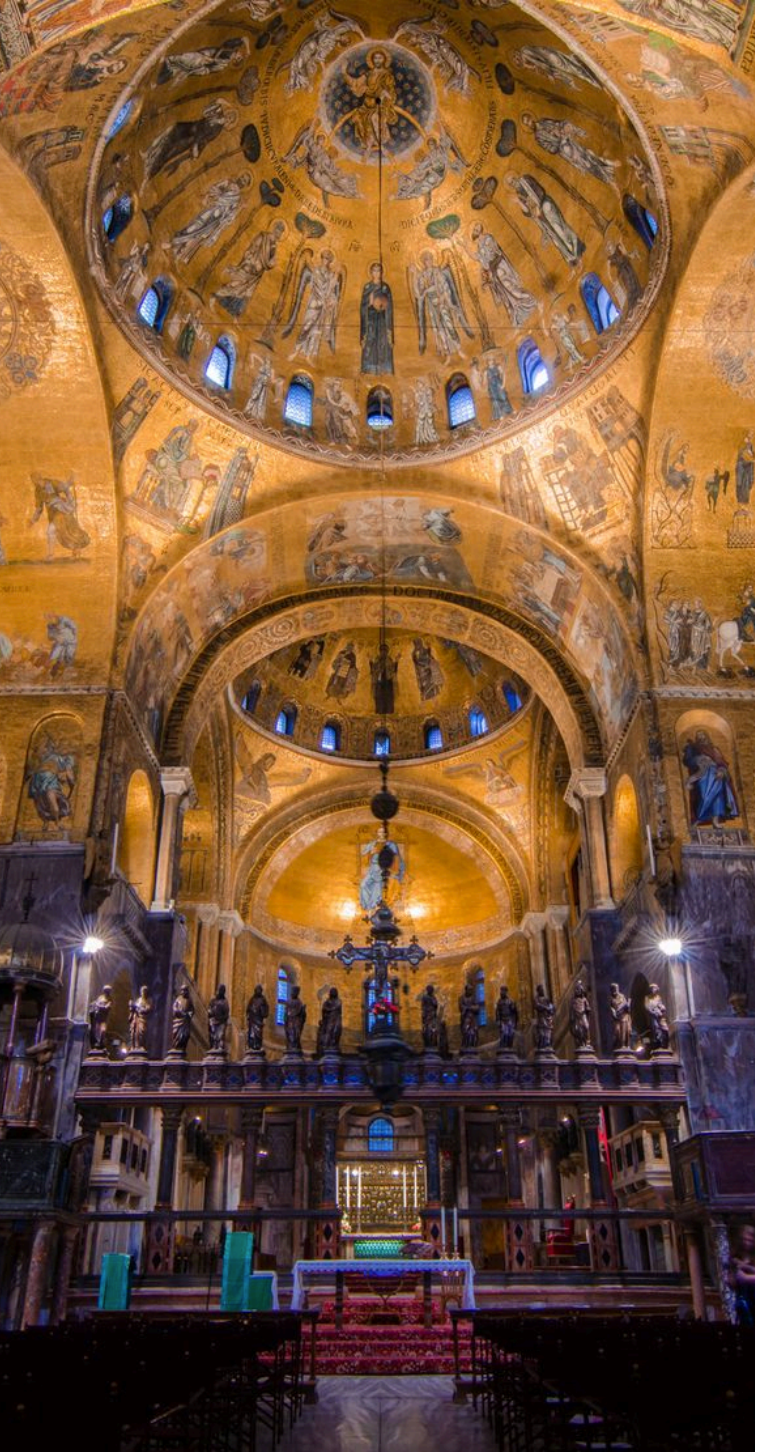
Many evolutionary innovations are non-adaptive

The spandrels of San Marco and the Panglossian paradigm: a critique of the adaptationist programme

By S. J. Gould and R. C. Lewontin

Museum of Comparative Zoology, Harvard University, Cambridge, Massachusetts 02138, *U.S.A.*

An adaptationist programme has dominated evolutionary thought in England and the United States during the past 40 years. It is based on faith in the power of natural selection as an optimizing agent. It proceeds by breaking an organism into unitary 'traits' and proposing an adaptive story for each considered separately. Trade-offs among competing selective demands exert the only brake upon perfection; non-optimality is thereby rendered as a result of adaptation as well. We criticize this approach and attempt to reassert a competing notion (long popular in continental Europe) that organisms must be analysed as integrated wholes, with *Baupläne* so constrained by phyletic heritage, pathways of development and general architecture that the constraints themselves become more interesting and more important in delimiting pathways of change than the selective force that may mediate change when it occurs.



Brodsky, Thattai & Mayor, Nat Cell Biol 2012
Ramadas & Thattai, Biophys J 2013
Purkanti & Thattai, PNAS 2015
Mani & Thattai, Mol Biochem Parasitol 2016
Dey, Thattai & Baum, Trends Cell Biol 2016
Mani & Thattai, eLife 2016
Shukla et al, PLoS ONE 2017 (in rev.)

NCBS:
Rohini Ramadas, Ramya Purkanti, Somya Mani, Anjali Jaiman, Shruti Malviya, Sachit Daniel

Collaborators:
UCL: Gautam Dey, Buzz Baum
CMI: Ankit Shukla, Mandayam Srivas, Madhavan Mukund, Shyamlal Karra
IISc: Arnab Bhattacharyya
ISI: Kesav Krishnan

Mukund Thattai:
thattai@ncbs.res.in, @thattai

Simons @ NCBS

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