

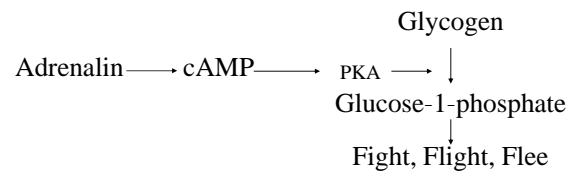
Complex Aspects of Cell Signaling

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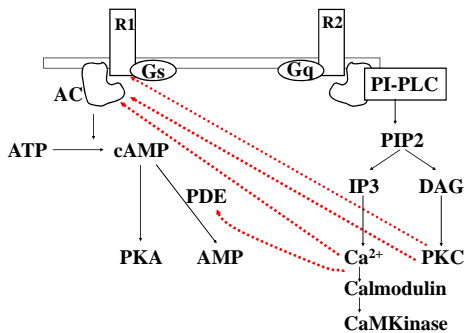
The Purpose of Teaching is Learning

Intracellular Signaling

- Linear information transfer
- Signaling networks

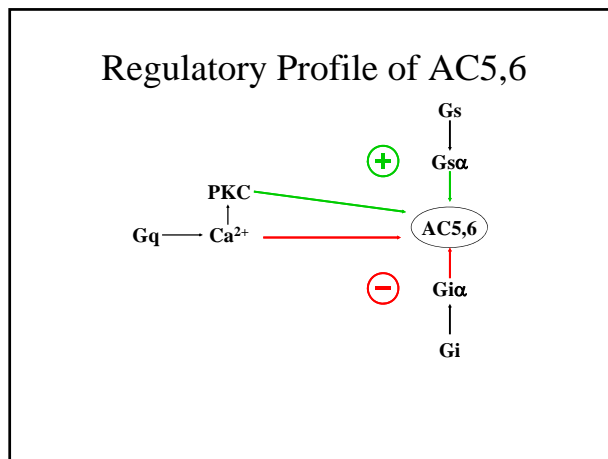
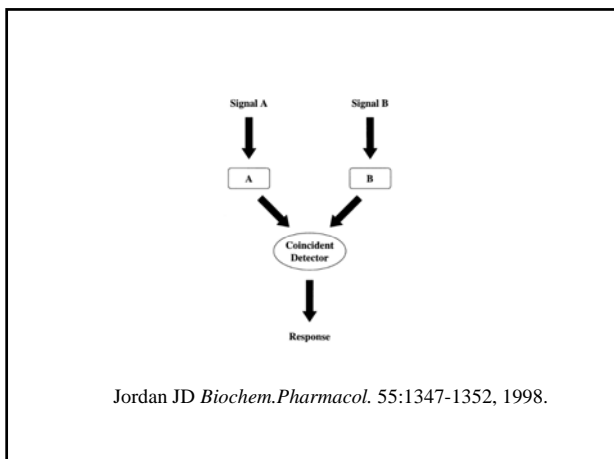


Network



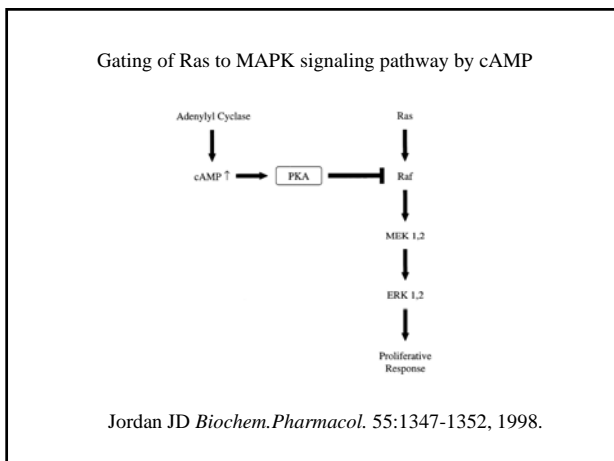
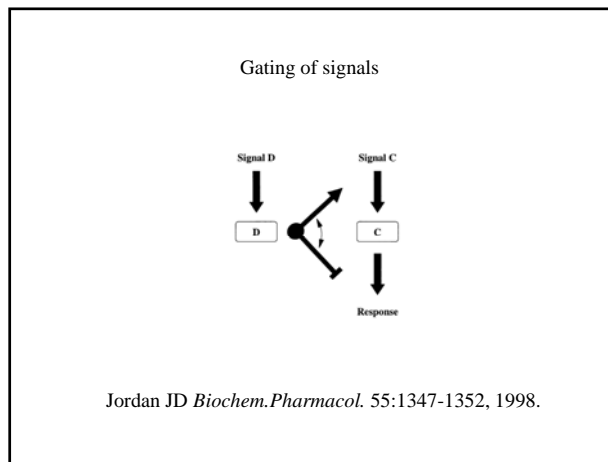
Examples of interactions in signalling network

- Co-incidence detection



Examples of interactions in signalling network

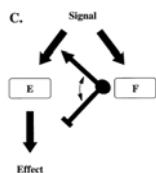
- Gating



Examples of interactions in signalling network

- Feedback loop

Feedback of signals

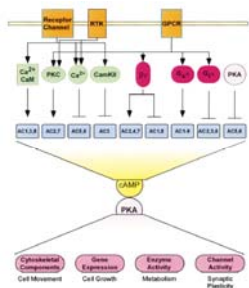


Jordan JD *Biochem.Pharmacol.* 55:1347-1352, 1998.

Components of Signaling Networks

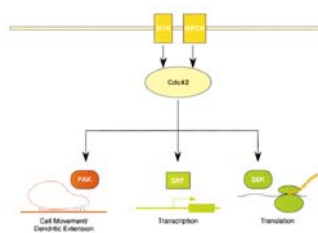
- **Junctions:** Integrators
- **Nodes:** split and route signals

Example of a junction

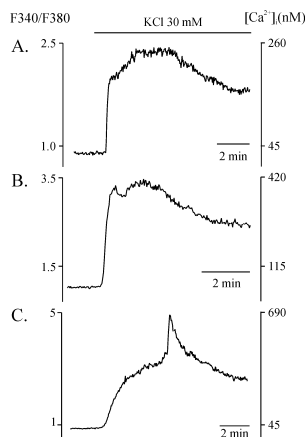


Jordan JD *Cell* 103:193-200, 2000.

Example of a node



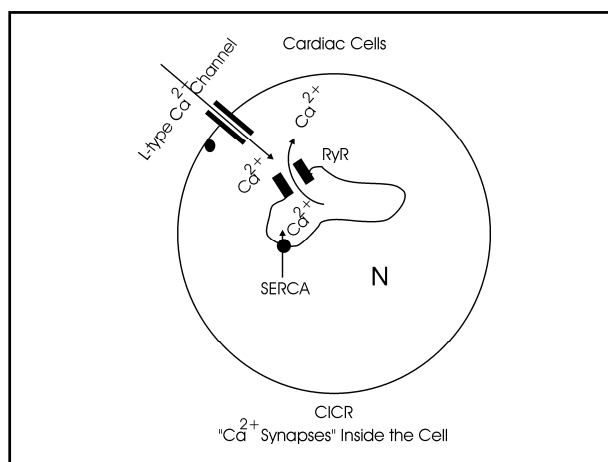
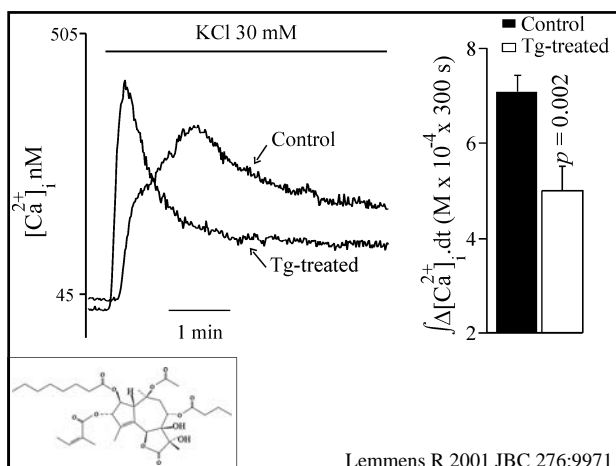
Jordan JD *Cell* 103:193-200, 2000.



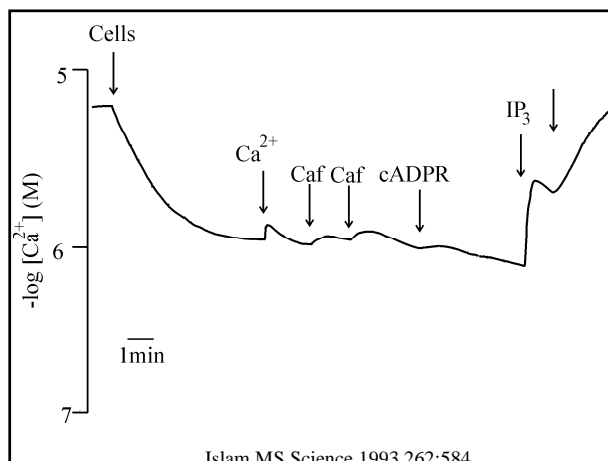
Lemmens R 2001
JBC 276: 9971

Logic

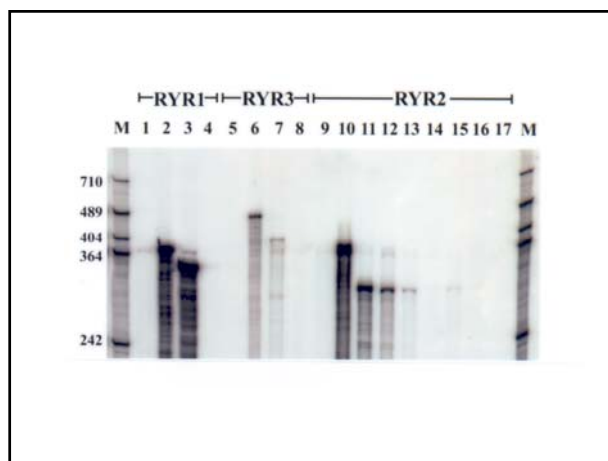
- $A \rightarrow B$
- $A \rightarrow C$
-
- $B \rightarrow C$

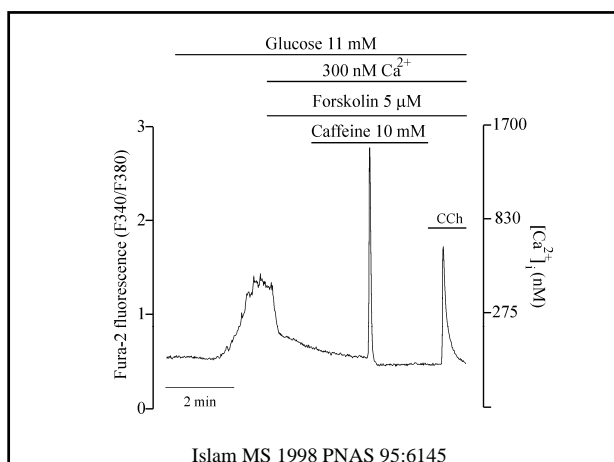


Voltage-gated Ca²⁺ channels
Ca²⁺-gated Ca²⁺ channels
*IP₃ receptor
*Ryanodine Receptor
*Polycystin-2



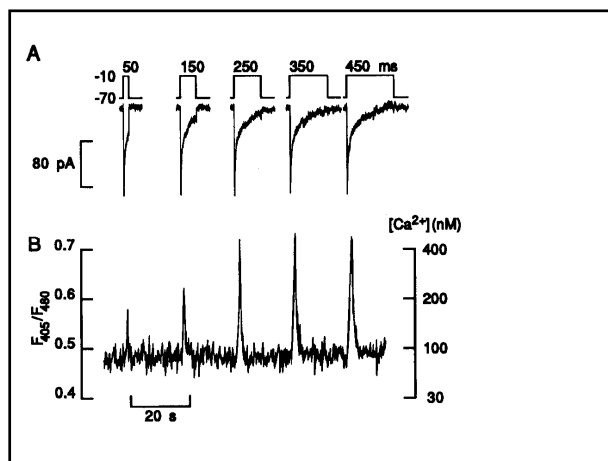
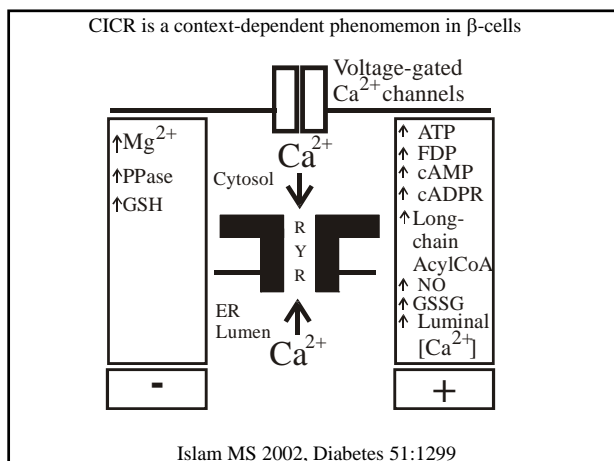
679
Biochem. J. (1995) 308, 679-686 (Printed in Great Britain)
Effects of caffeine on cytoplasmic free Ca²⁺ concentration in pancreatic β-cells are mediated by interaction with ATP-sensitive K⁺ channels and L-type voltage-gated Ca²⁺ channels but not the ryanodine receptor
Md. Shahidul ISLAM,
The Roll Luit Center for Diabetes Research, Department of Molecular Medicine, Karolinska Institute, Karolinska Hospital, S-171 76 Stockholm, Sweden





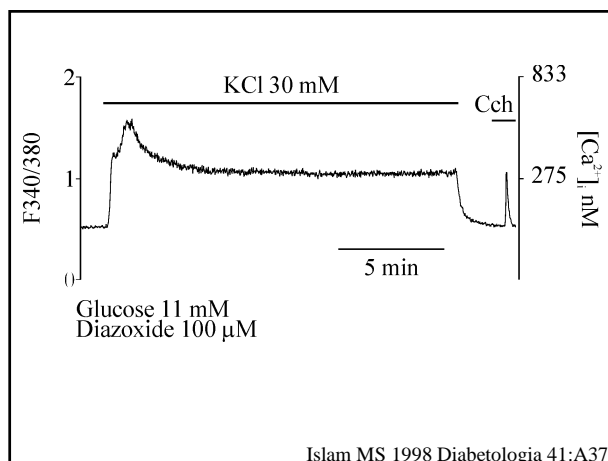
”Unlock” the gate and then
”Open” it

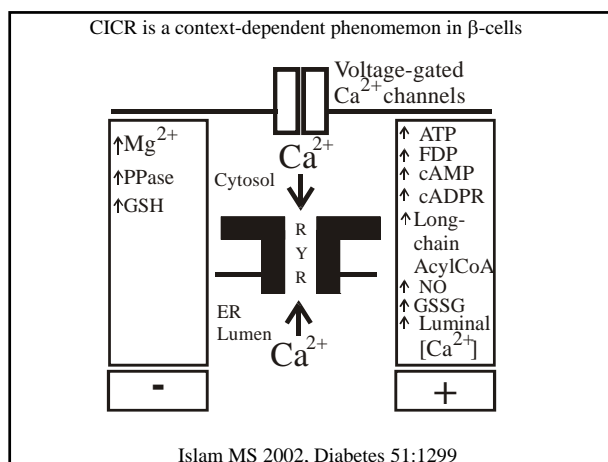
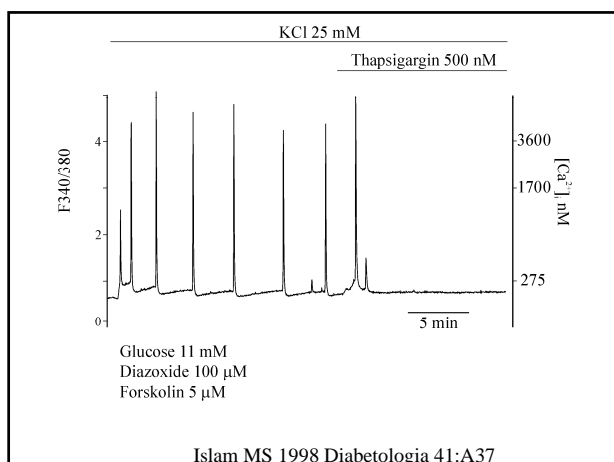
- Mg²⁺ and FKBP12.6 constitute the ”lock”
- PKA ”Unlocks” RyR
 - By relieving Mg²⁺ inhibition
 - By dissociating FKBP12.6
 - By promoting filling of ER
- Functional RY2 is a phosphoprotein
- Ca²⁺ ”Opens” RyR



Problems with patch-clamp experiments

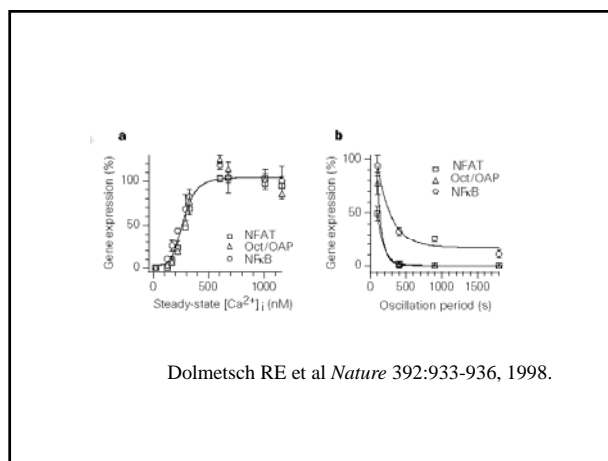
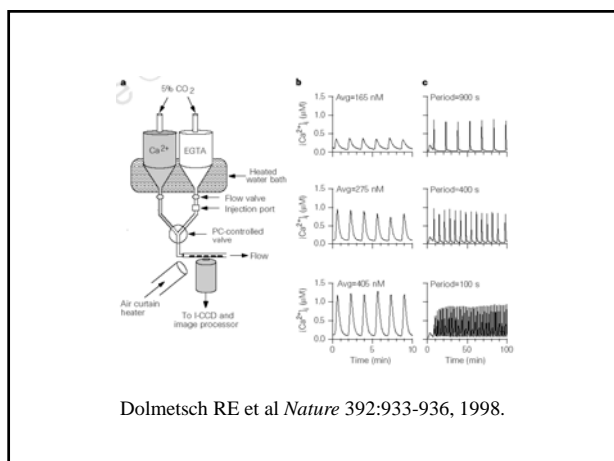
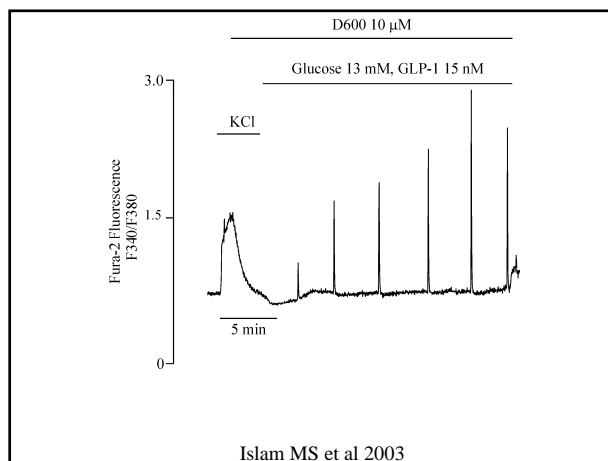
- High extracellular Ca²⁺
- High intracellular Ca²⁺ chelators
- 100 mM CsCl (Blocks RyR receptors)
- 20 mM TEA (Blocks RyR receptors)
- Dialysis
- Others





Receptors linked to

- PI-PLC (Ca^{2+} signals)
- AC (cAMP signal)



Thoughts on Emergence

- High-level properties of a system that are simply not deducible from its low-level properties
- Properties of a system that are not possessed by any of its parts
- Phenomenon wherein complex, interesting high-level function is produced as a result of combining simple low-level mechanisms in simple ways.

(From David J Chalmers philosopher at Univ of Arizona)

Emergent properties of signalling networks

Signalling networks have capabilities and properties that cannot be readily predicted from known properties of the component molecules.

Examples of Emergent Properties of Signaling

- Prolongation of signalling and information storage in the network
- Integration of signals across different time scales
- Generation of different outputs depending on strength and duration of the input

(Bhalla US, *Science* 1999, **283**:381-387)

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