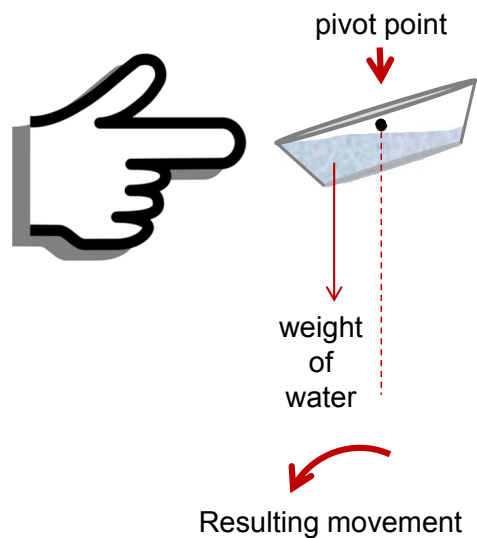# Positive feedback and bistability in MAP kinase pathways generates memory

Positive feedback is a requirement for bistability

Positive feedback is a "runaway" process, where an effect enhances itself.

After a small perturbation, water moving tips the bucket and causes the water to move more and so tips the bucket further.

If an increase in the output of the system increases the output of the system still further, then the system has positive feedback.

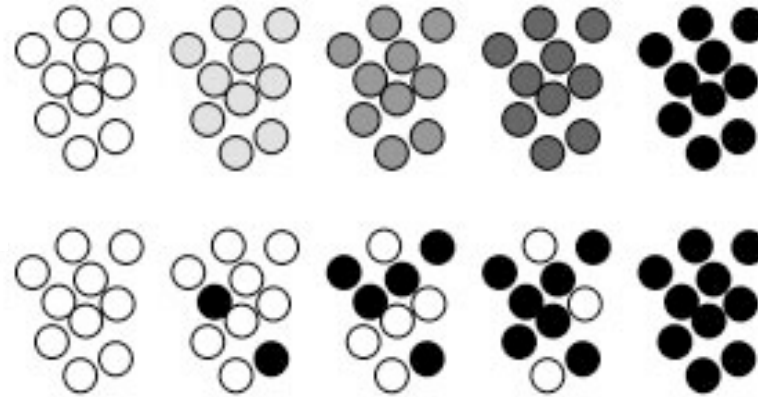# Bistability underlies the maturation of frog oocytes.
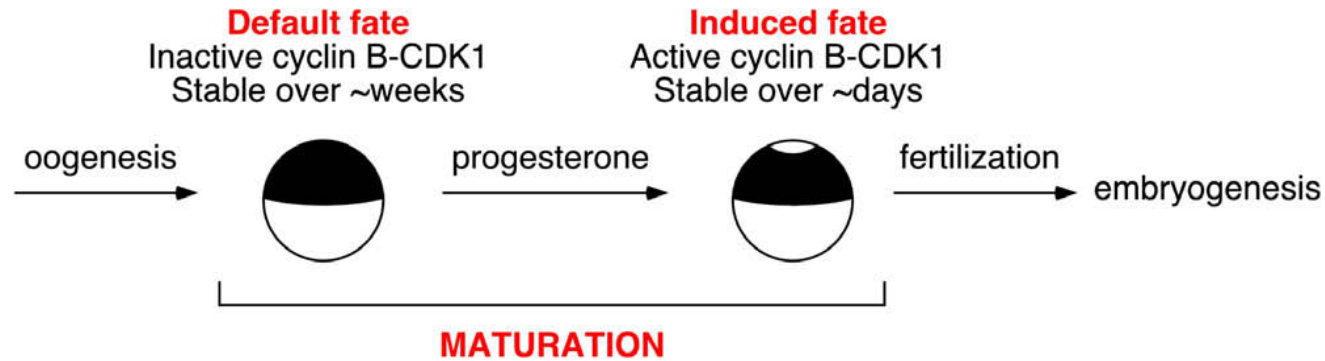
The bistability is generated by an ultrasensitive, MAP kinase cascade and positive feedback.
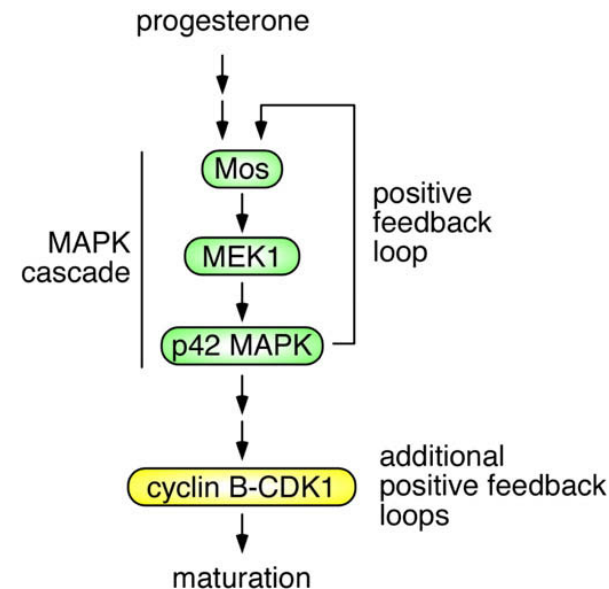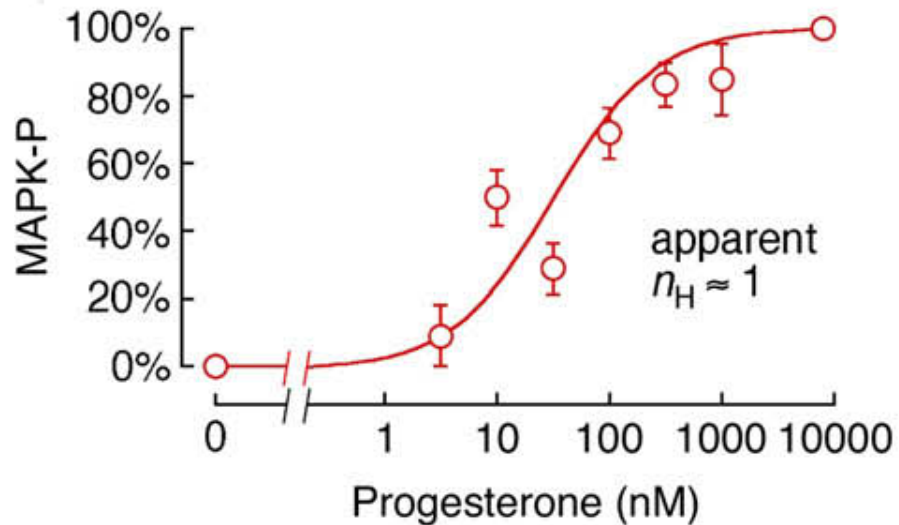
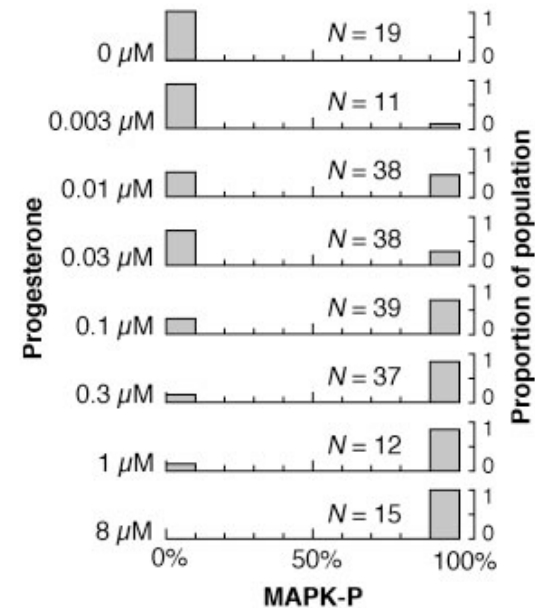# We need to look at single cells to see switching

The same average behaviour of a population can be generated by different behaviours in single cells.

Population level measurements of activated MAP kinase

Single-cell level measurements of activated MAP kinase

Ultrasensitivity in the mitogen-activated protein kinase cascade

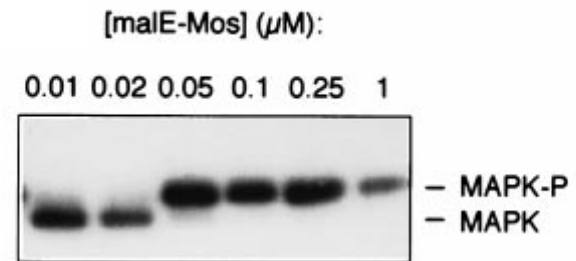CHI-YING F. HUANG AND JAMES E. FERRELL, JR.†

Requiring two phosphorylations to become active and distributive phosphorylation generates an ultrasensitive response that becomes more ultrasensitive with each step of the cascade.
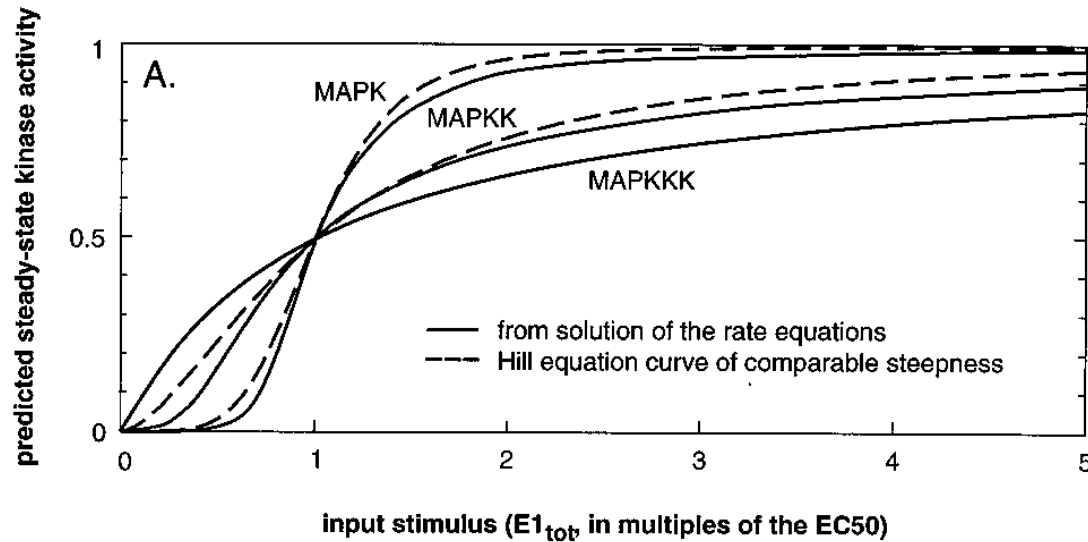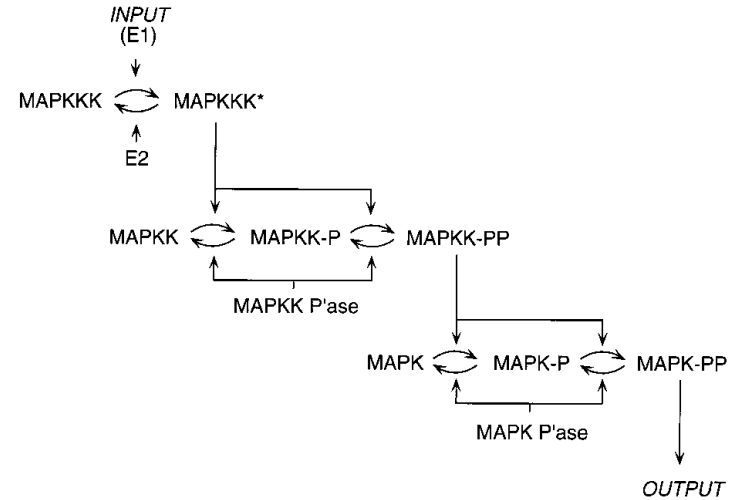
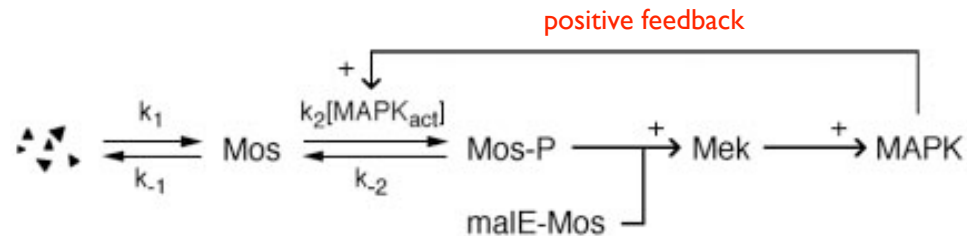# Ultrasensitivity does increase down the MAPK cascade
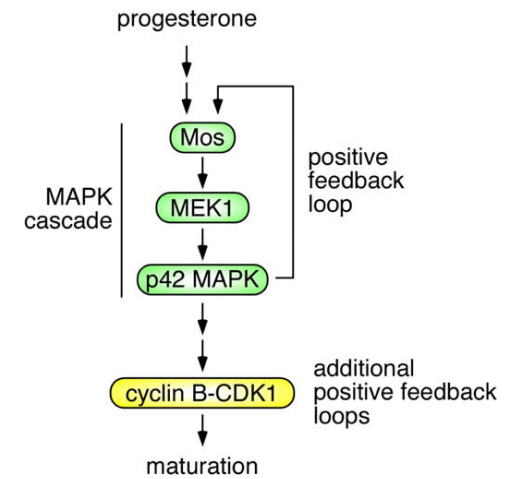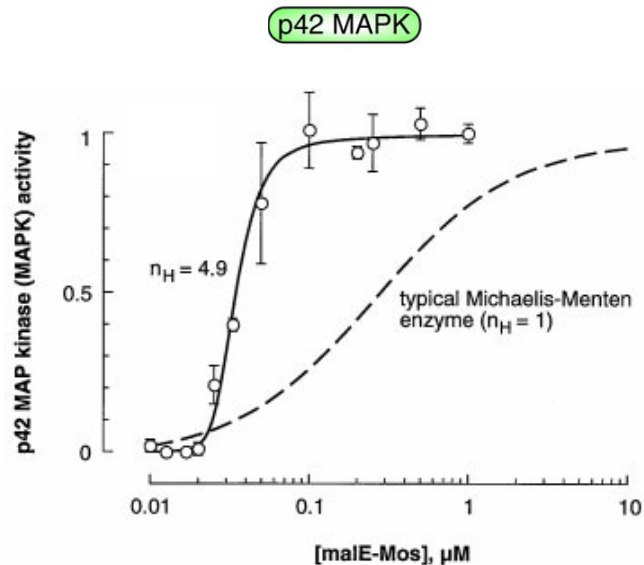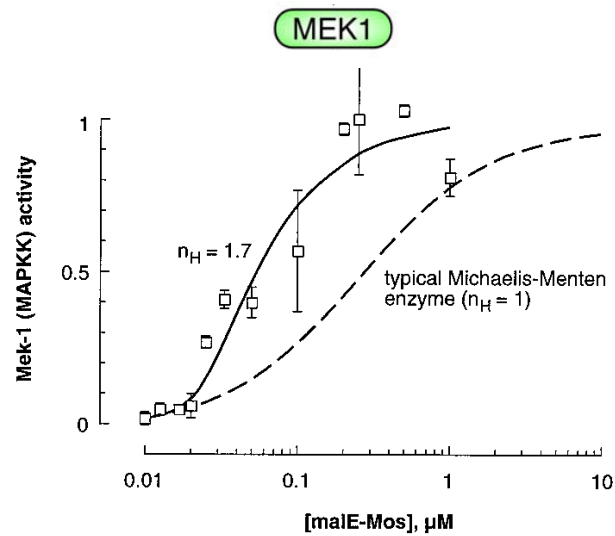
Levels of active kinases were measured using Western blots.

malE-Mos is an exogenously expressed version of Mos.

Positive feedback is also present and is required for bistable, or "all-or-none", behaviour

positive feedback

$$\text{triangles} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \text{Mos} \underset{k_{-2}}{\overset{k_2[\text{MAPK}_{\text{act}}]}{\rightleftharpoons}} \text{Mos-P} \xrightarrow{+} \text{Mek} \xrightarrow{+} \text{MAPK}$$
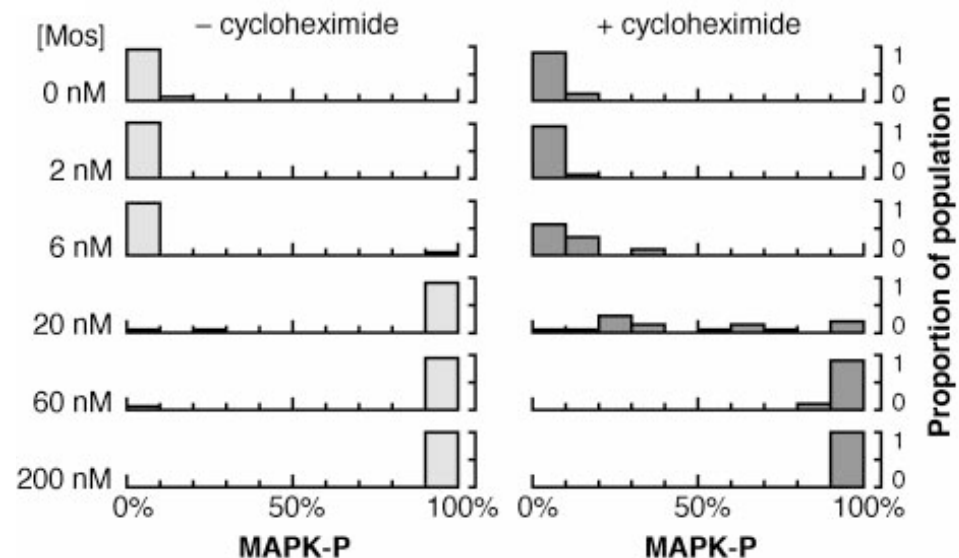
malE-Mos

The Biochemical Basis of an All-or-None Cell Fate Switch in *Xenopus* Oocytes

James E. Ferrell Jr.* and Eric M. Machleder

With cycloheximide, which inhibits translation, bistability, but not ultrasensitivity, is lost.

Positive feedback requires the synthesis of new proteins.

The p42 MAP kinase becomes more active as levels of progesterone increase.