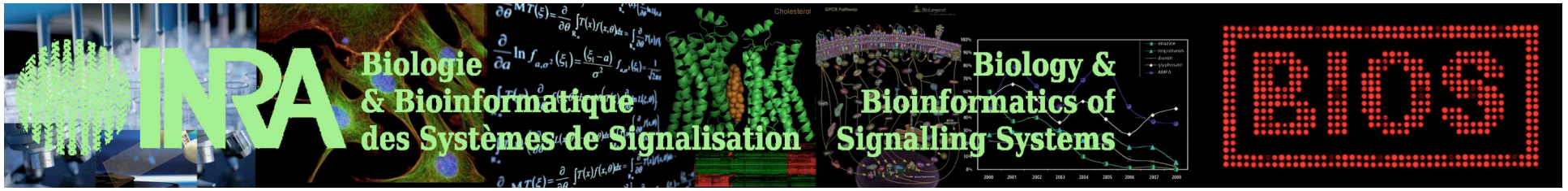

Inference of Biological Networks from Experimental Data

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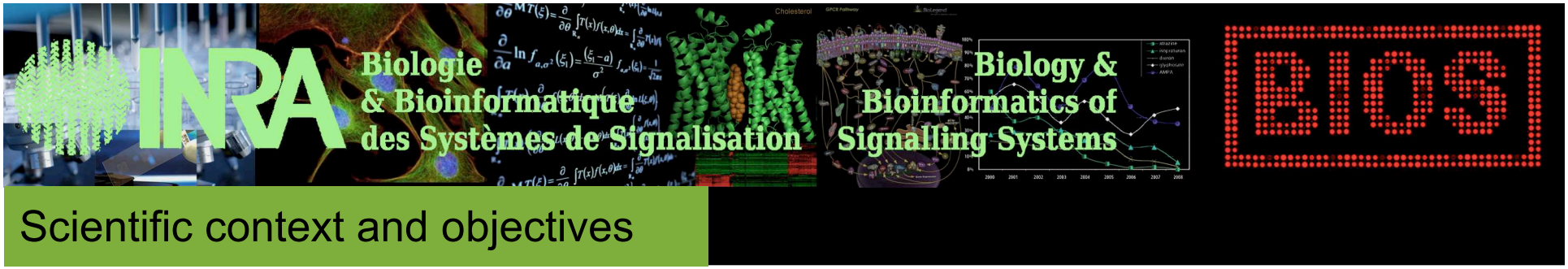
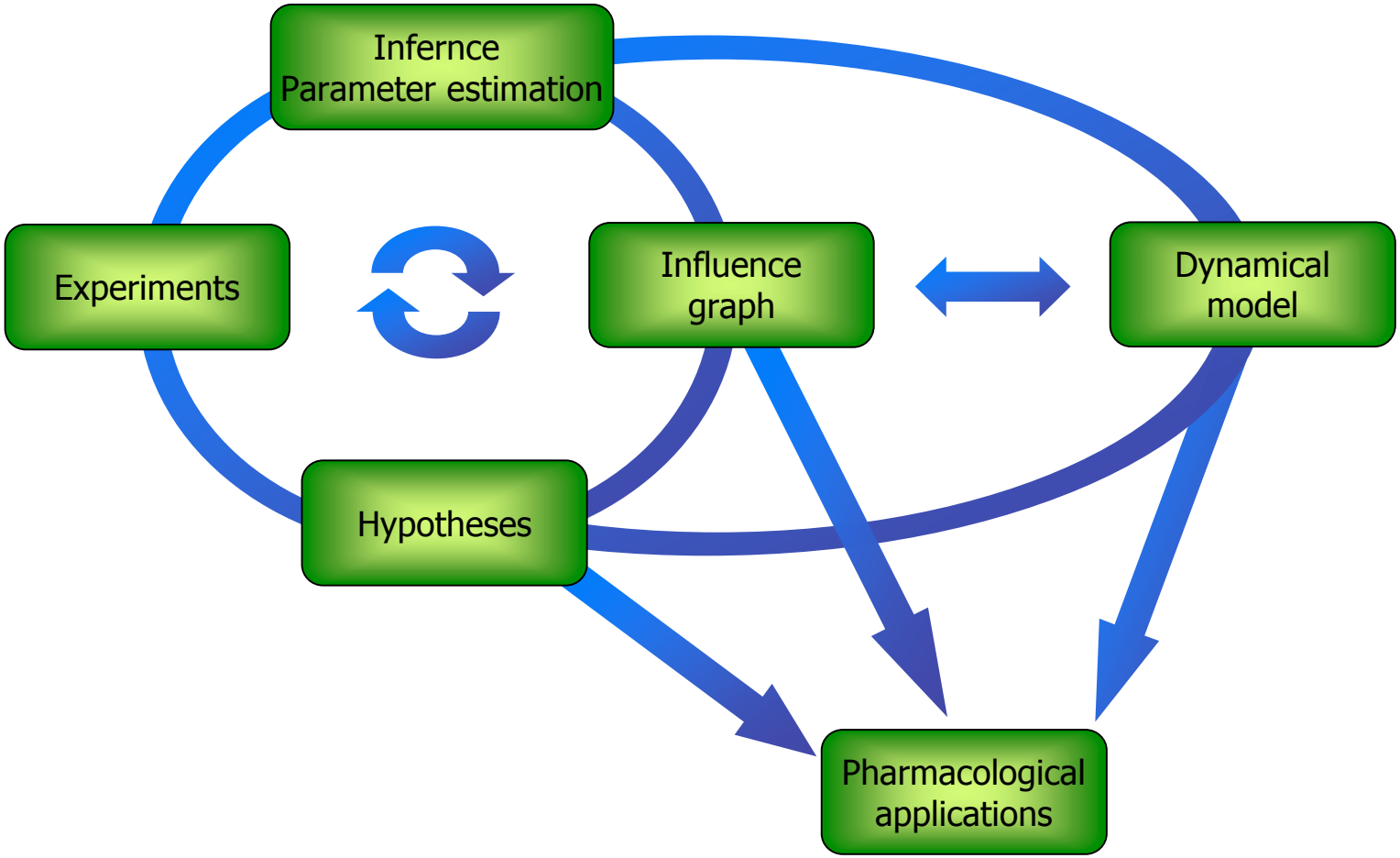


Scientific context and objectives

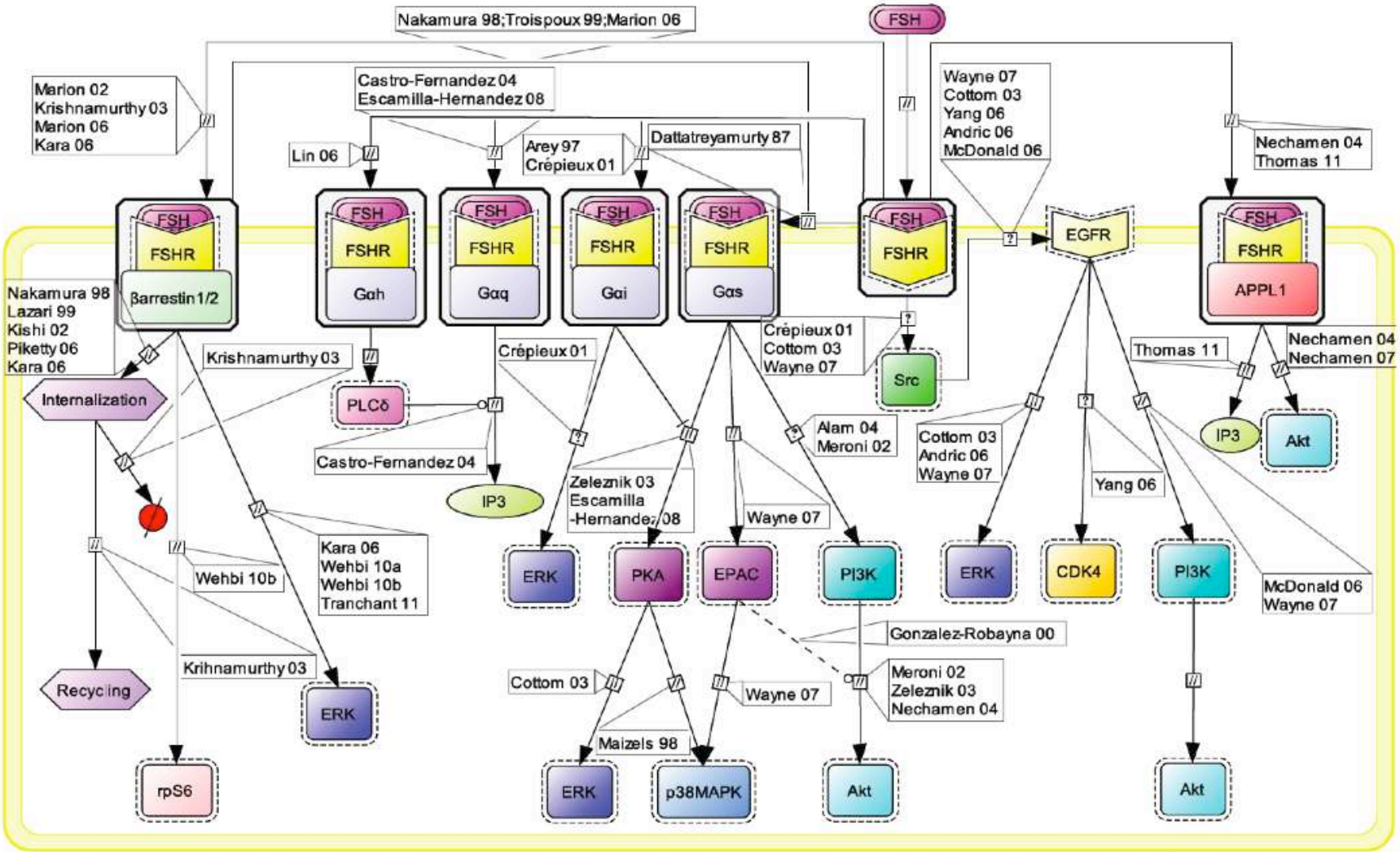
To develop the bioinformatics tools necessary for modelling signalling networks.

- Understand how the system works
- Understand why sometimes it doesn't work
- What should be done to come back to normal behaviour
- Estimate *in silico* the effect of a molecule
- Build better activity screens

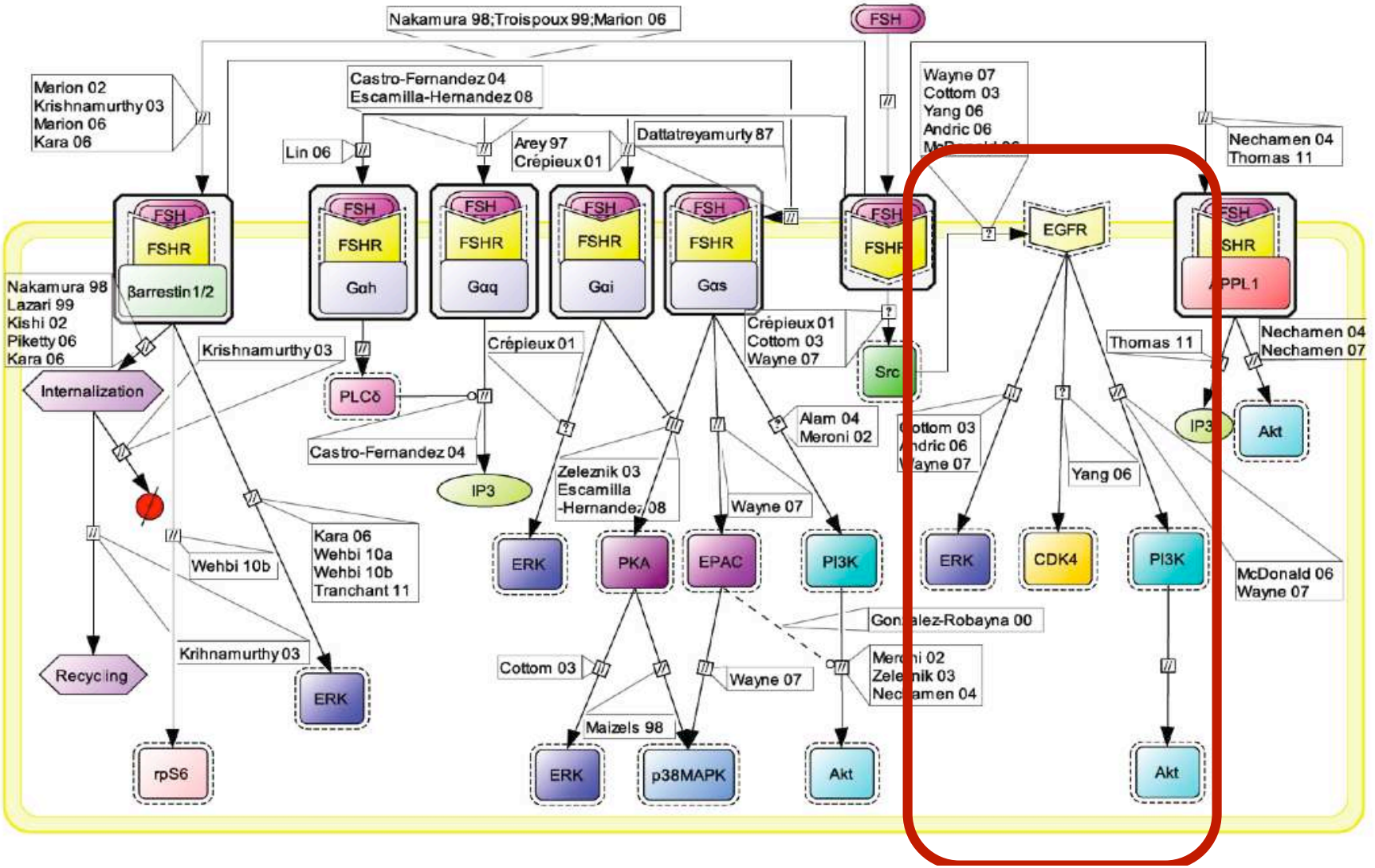
Scientific context and objectives



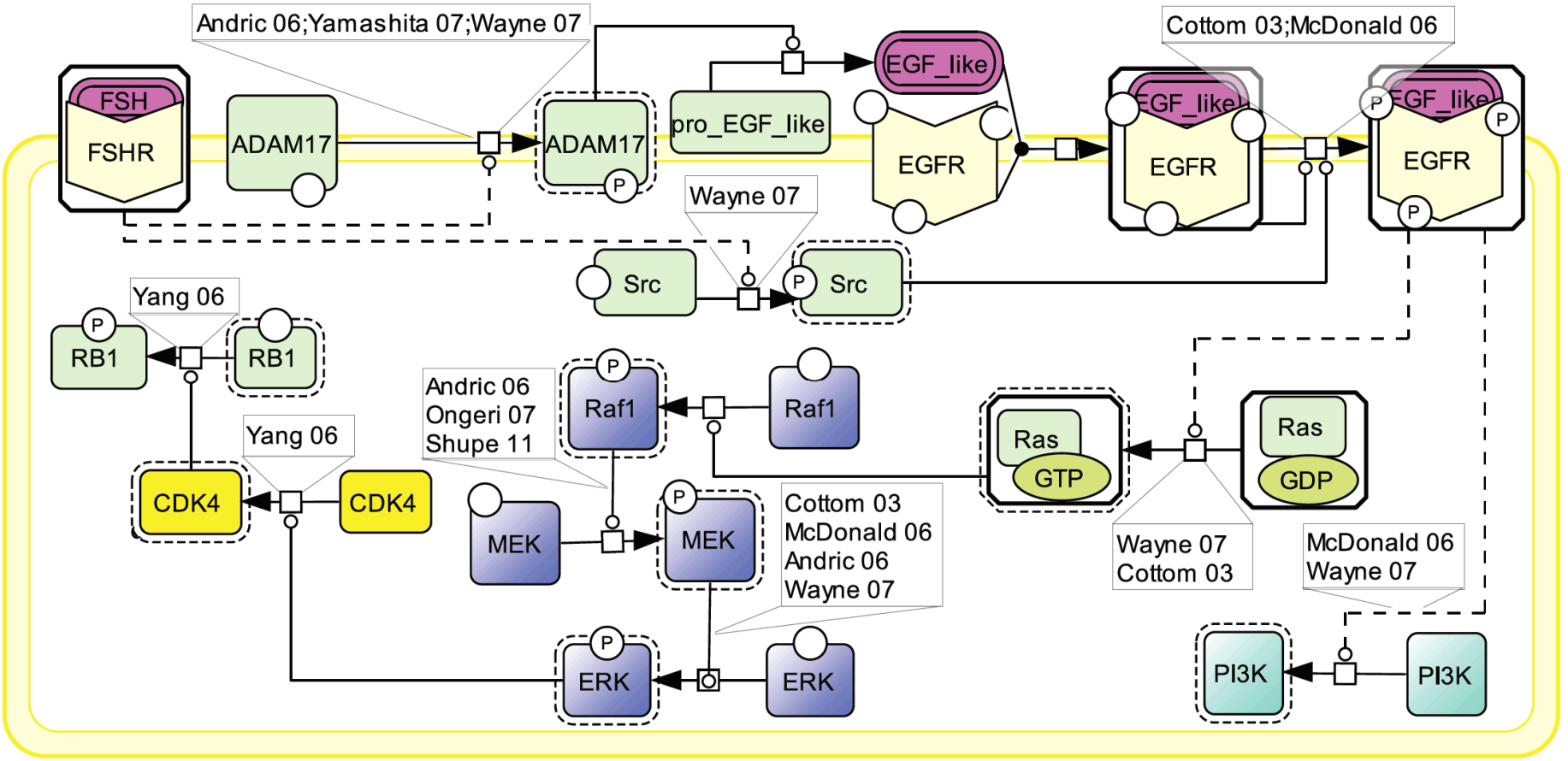
Scientific context and objectives



Scientific context and objectives

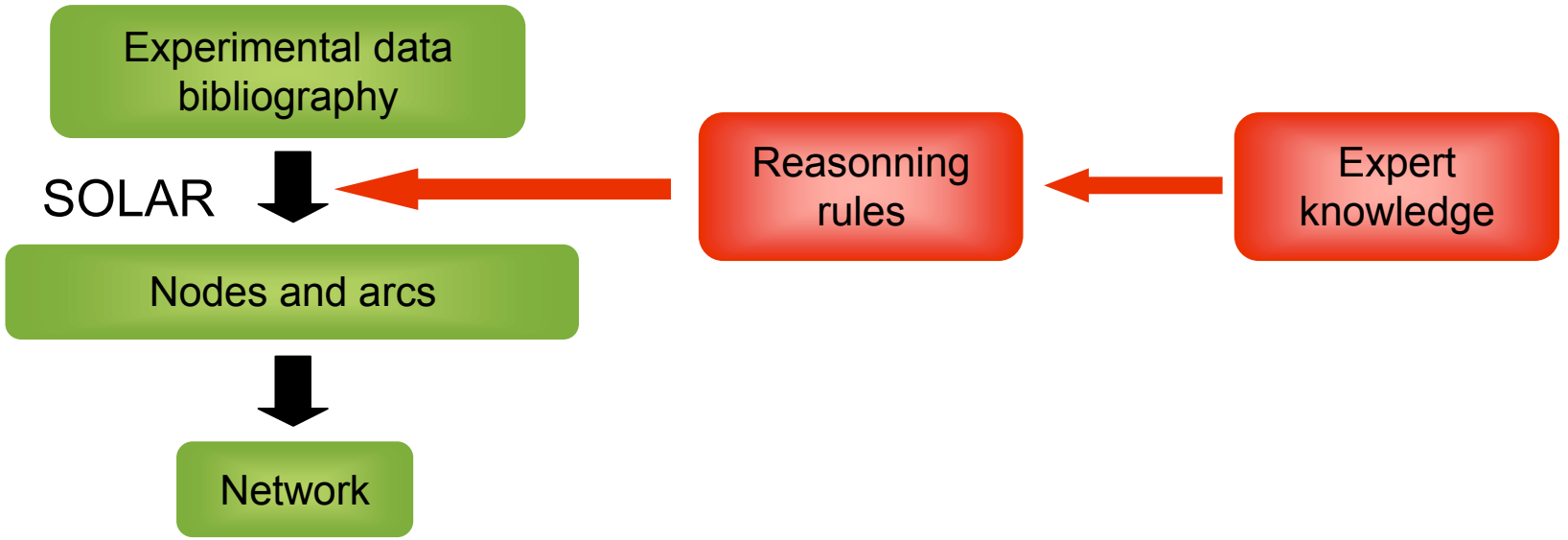


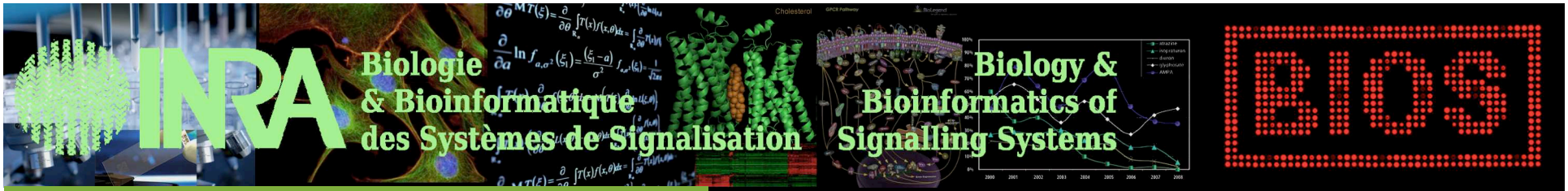
Scientific context and objectives



Principle of the method

Objective: An automated method that can deduce the network from the experimental data. Knowledge-based method.





Development

Rules

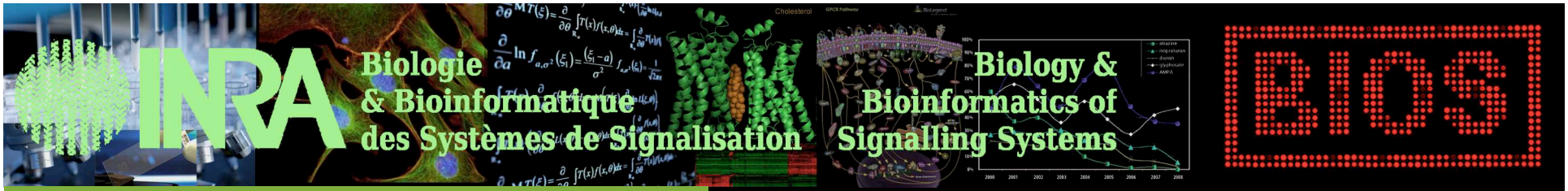
- Primary rules: direct deductions from experimental data
  9 experiment types formalized

- Secondary rules: at least one of the conditions is the conclusion of a primary rule
  More than 300 rules

- Admitted facts.

Inference

Strictly deductive, using SOLAR



Development

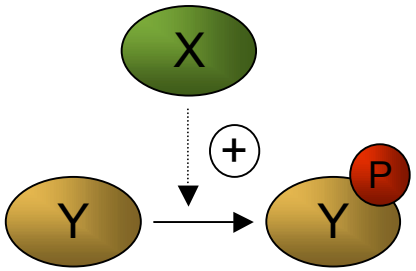
Primary rules
Direct deductions from experiments

Example: The phosphorylation level of the protein ERK was measured by western blot in control conditions and in the presence of FSH at cell surface. It was found higher when FSH is present. We can deduce from this experiment that FSH increases the propshorylation level of ERK.

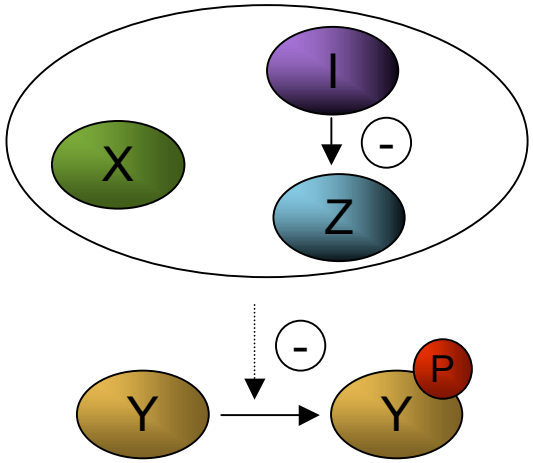
More generally:

IF WB(x, a, b, increase) AND modified(a, y) AND antibody(b, a)
THEN ACTIVATES(x, y, a, unknown, confirmed, increase)

Seconday rules
Combining conclusions

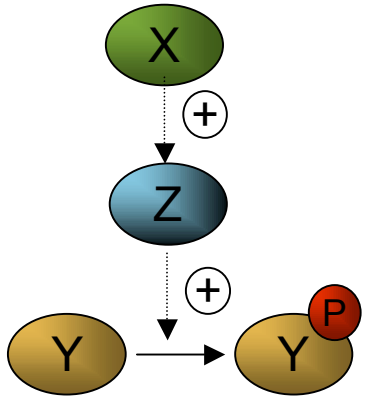


IF x activates y

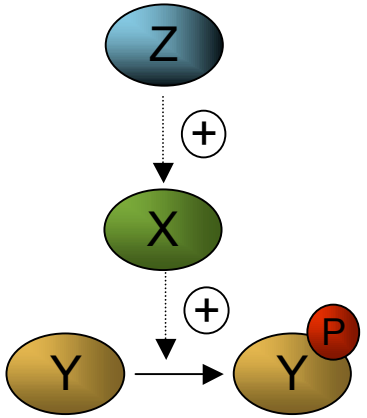


AND z abolishes activation

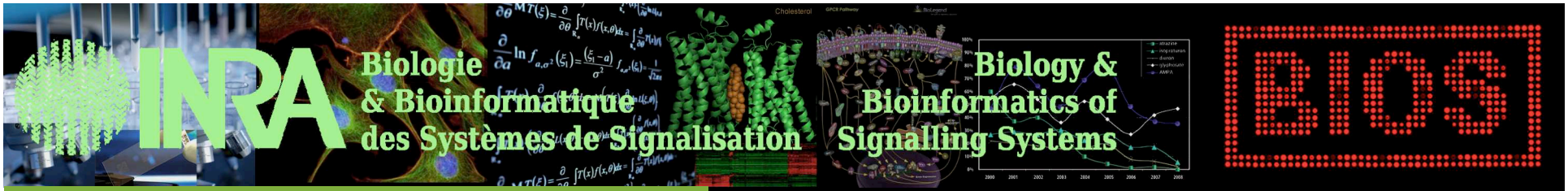
THEN



OR



IF	x activates y
AND	inhibitor of z abolishes activation
THEN	(x activates z AND z activates y)
	OR (z activates x AND x activates y)



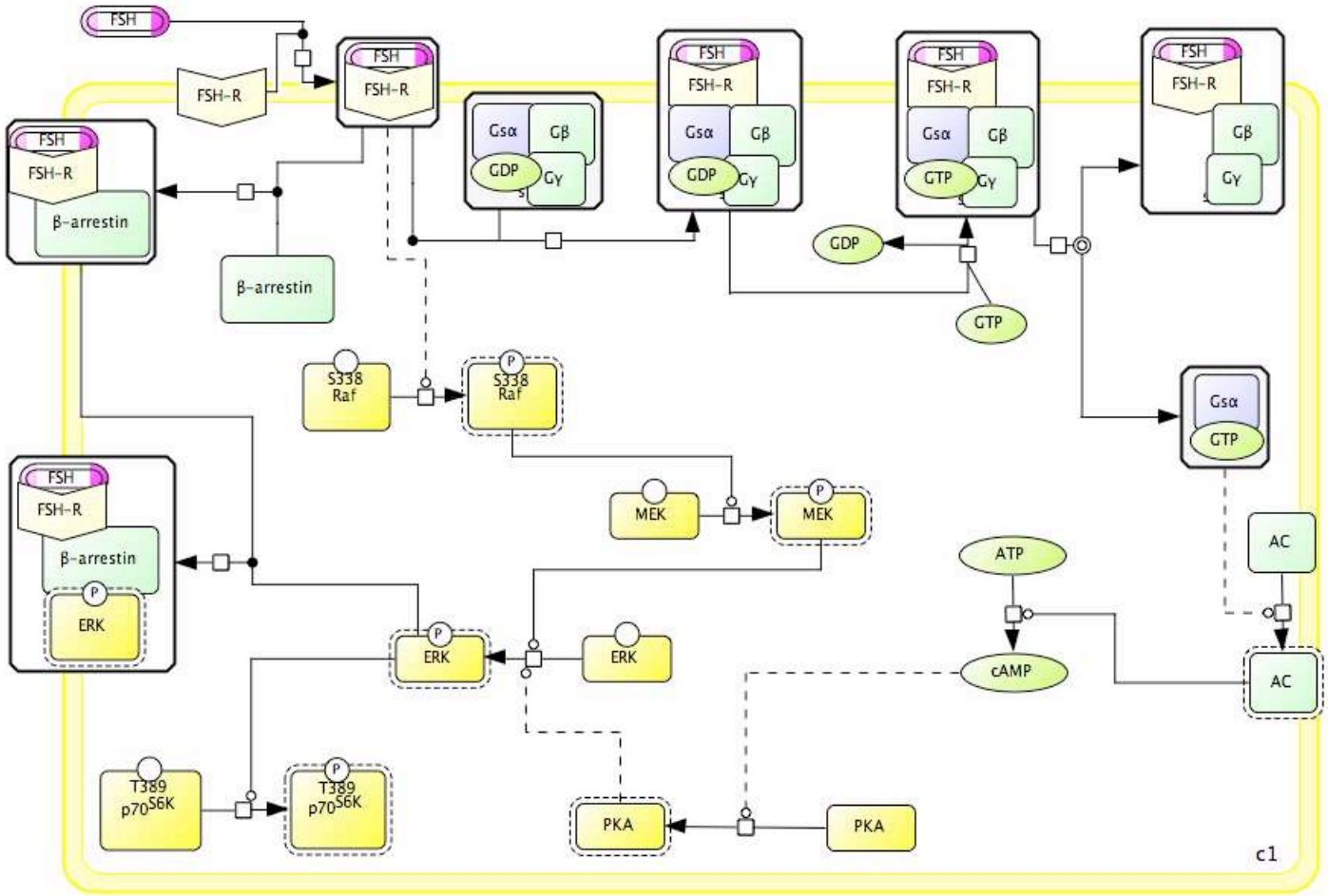
Development

Admitted facts

- Old experiments difficult to formalize (and maybe not useful…)
- Things we can be reasonably sure about
- Background knowledge

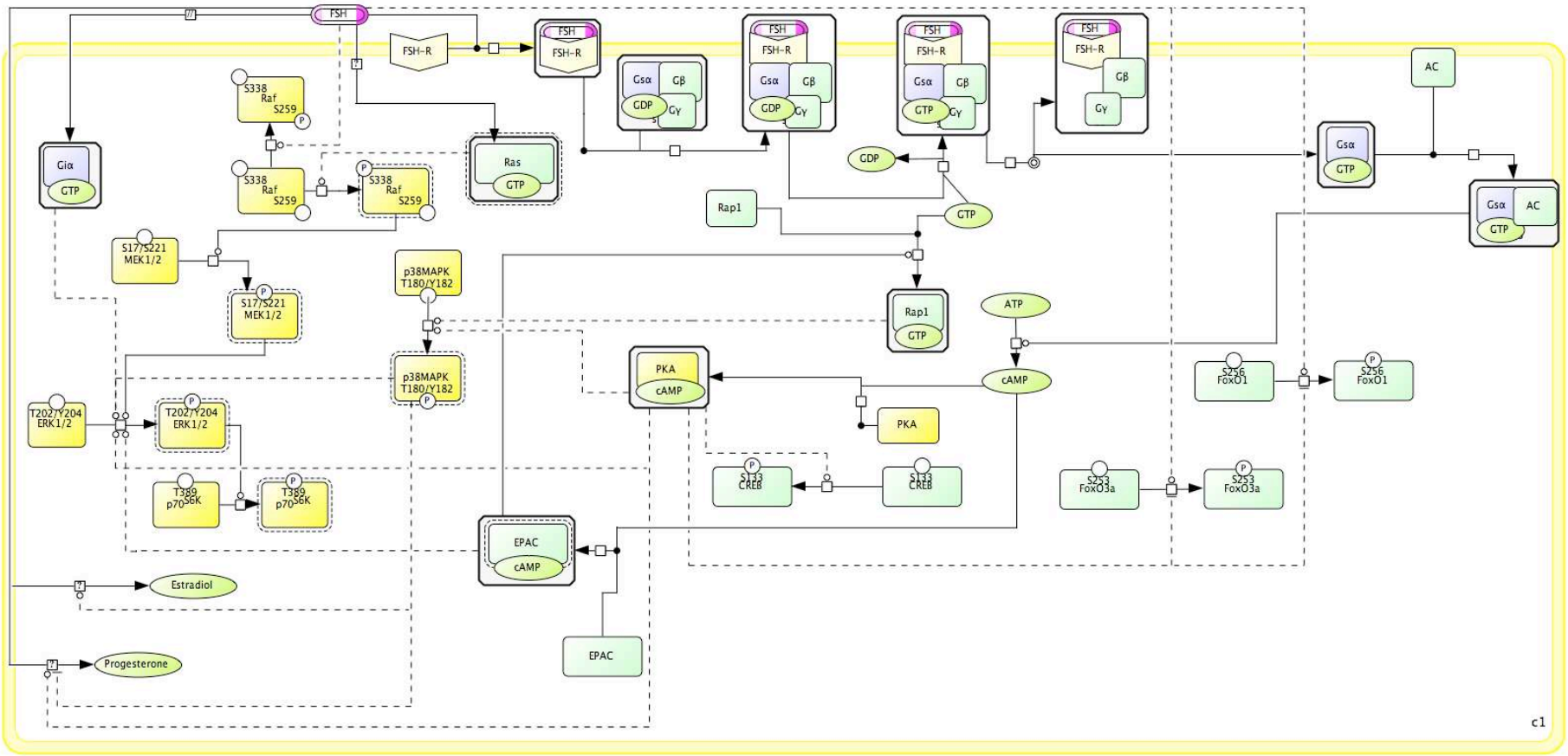
Development

52 facts, all reactions are found, no new conclusions.



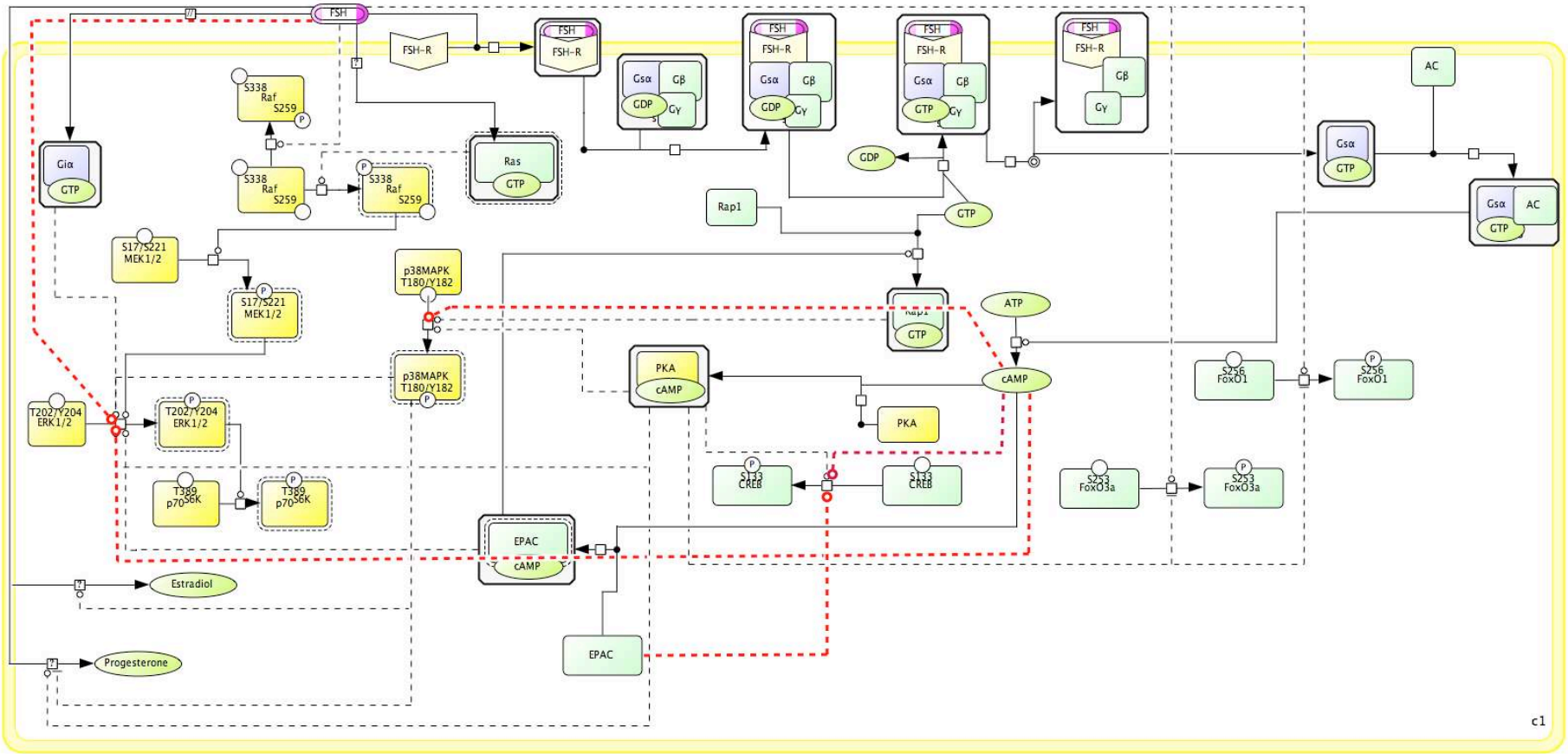
Development

Input: 302 facts

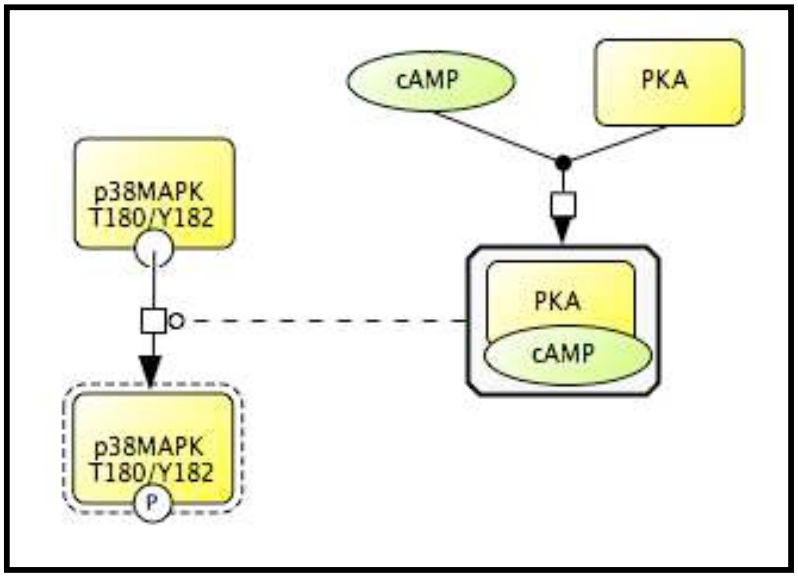


Development

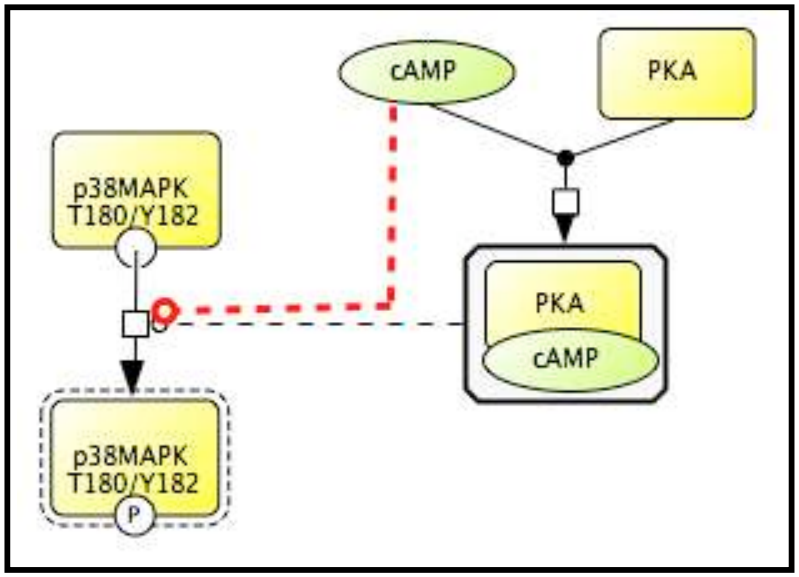
Output: 12 « new » facts.



Development

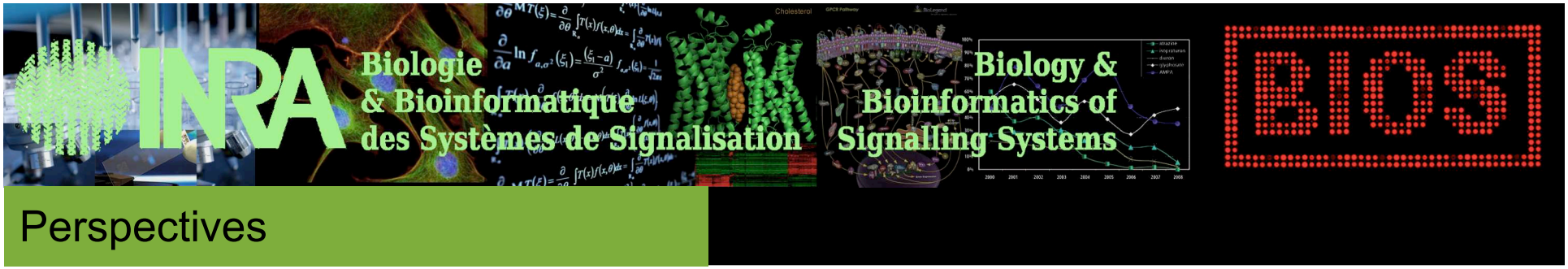


Expected



Inferred

New fact is neither false, nor truly unexpected !
We should introduce « prunning ».



Perspectives

• Enlarge application domain: add new experiment types, new primary rules

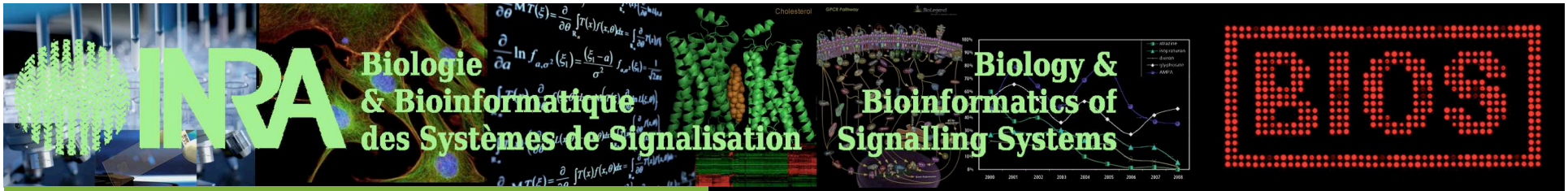
• Many secondary rules are needed.

• Conflicts management.

When experimental data lead to contradictory conclusions. Will be bease on reliability of experimental protocol, number of publications, level, etc.

• Abduction and meta-abduction

What experiment should be made to demonstrate a given fact ?
What will I learn if I do this experiment ?



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