

<< **mathsbml.m**

MathSBML 2.2.1-beta-17 (25-Feb-2004) loaded 27-February-2004 18:40:55.207488

MAP-K Cascade

With negative feedback

Based on the model in:

Kholodenko, B. M. (2000) Negative feedback and ultrasensitivity can bring about oscillations in the mitogen-activated protein kinase cascades. *Eur. J. Biochem.* **267**: 1583-1588.

Create the Model with the Model Builder

```

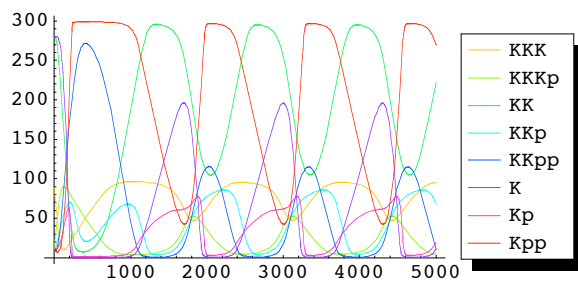
newModel[id → "MAPK", name → "MAPK with feedback [Kholodenko,2000]", echo → False];
addCompartment[uVol];
addSpecies[KKK, initialAmount → 90];
addSpecies[KKKp, initialAmount → 10];
addSpecies[KK, initialAmount → 280];
addSpecies[KKp, initialAmount → 10];
addSpecies[KKpp, initialAmount → 10];
addSpecies[K, initialAmount → 280];
addSpecies[Kp, initialAmount → 10];
addSpecies[Kpp, initialAmount → 10];
addReaction[KKK → KKKp, kineticLaw → V1 * KKK / ((1 + (Kpp / Ki) ^ n) * (K1 + KKK)),
  parameters → {V1 → 2.5, Ki → 10, n → 1, K1 → 10}, modifiers → Kpp, reversible → False];
addReaction[KKKp → KKK, kineticLaw → V2 * KKKp / (KK2 + KKKp),
  parameters → {V2 → 0.25, KK2 → 8}, reversible → False];
addReaction[KK → KKp, kineticLaw → k3 * KKKp * KK / (KK3 + KK),
  modifiers → KKKp,
  parameters → {k3 → 0.025, KK3 → 15}, reversible → False];
addReaction[KKp → KKpp, kineticLaw → k4 * KKKp * KKp / (KK4 + KKp),
  modifiers → KKKp,
  parameters → {k4 → 0.025, KK4 → 15}, reversible → False];
addReaction[KKpp → KKp, kineticLaw → V5 * KKpp / (KK5 + KKpp),
  parameters → {V5 → 0.75, KK5 → 15}, reversible → False];
addReaction[KKp → KK, kineticLaw → V6 * KKp / (KK6 + KKp),
  parameters → {V6 → 0.75, KK6 → 15}, reversible → False];
addReaction[K → Kp, kineticLaw → k7 * KKpp * K / (KK7 + K), modifiers → KKpp,
  parameters → {k7 → 0.025, KK7 → 15}, reversible → False];
addReaction[Kp → Kpp, kineticLaw → k8 * KKpp * Kp / (KK8 + Kp), modifiers → {KKpp},
  parameters → {k8 → 0.025, KK8 → 15}, reversible → False];
addReaction[Kpp → Kp, kineticLaw → V9 * Kpp / (KK9 + Kpp),
  parameters → {V9 → 0.5, KK9 → 15}, reversible → False];
addReaction[Kp → K, kineticLaw → V10 * Kp / (KK10 + Kp),
  parameters → {V10 → 0.5, KK10 → 15}, reversible → False];

```

```
createModel["MAPK.html"]
MAPK.html
```

Load the model into the simulate and run a simulation

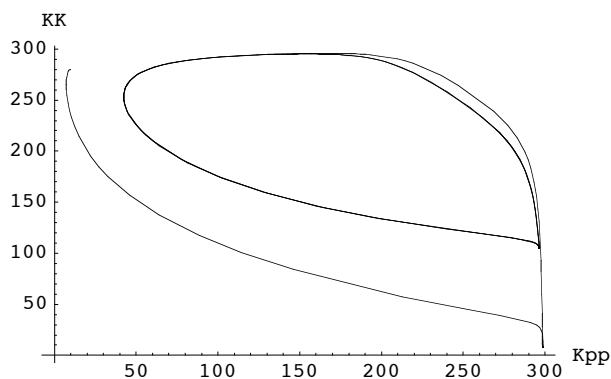
```
m = loadSimulator[context -> None];
s = SBMLNDSolve[m, 5000]
{{KKK[t] -> InterpolatingFunction[{{0., 5000.}}, <>][t],
  KKKp[t] -> InterpolatingFunction[{{0., 5000.}}, <>][t],
  KK[t] -> InterpolatingFunction[{{0., 5000.}}, <>][t],
  KKp[t] -> InterpolatingFunction[{{0., 5000.}}, <>][t],
  KKpp[t] -> InterpolatingFunction[{{0., 5000.}}, <>][t],
  K[t] -> InterpolatingFunction[{{0., 5000.}}, <>][t],
  Kp[t] -> InterpolatingFunction[{{0., 5000.}}, <>][t],
  Kpp[t] -> InterpolatingFunction[{{0., 5000.}}, <>][t]}}
SBMLPlot[s];
```



Use Standard *Mathematica* Features on Model

A Parametric Plot

```
ParametricPlot[Evaluate[{Kpp[t], KK[t]} /. s, {t, 0, 5000}, AxesLabel -> {"Kpp", "KK"}];
```



Display ODES in tabular Form

```
odes = SBMLODES /. m;
odes // TableForm
```

$$K' [t] == - \frac{0.025 K[t] K Kpp[t]}{15.+K[t]} + \frac{0.5 Kp[t]}{15.+Kp[t]}$$

$$KK' [t] == - \frac{0.025 KK[t] K Kp[t]}{15.+KK[t]} + \frac{0.75 K Kp[t]}{15.+K Kp[t]}$$

$$KKK' [t] == \frac{0.25 K K Kp[t]}{8.+K K Kp[t]} - \frac{2.5 K K K[t]}{(10.+K K K[t]) (1+0.1 Kpp[t]^1.)}$$

$$K K K p' [t] == - \frac{0.25 K K K p[t]}{8.+K K K p[t]} + \frac{2.5 K K K[t]}{(10.+K K K[t]) (1+0.1 Kpp[t]^1.)}$$

$$K K p' [t] == \frac{0.025 K K[t] K K p[t]}{15.+K K[t]} - \frac{0.75 K K p[t]}{15.+K K p[t]} - \frac{0.025 K K K p[t] K p[t]}{15.+K K p[t]} + \frac{0.75 K K p p[t]}{15.+K K p p[t]}$$

$$K K p p' [t] == \frac{0.025 K K K p[t] K p[t]}{15.+K K p[t]} - \frac{0.75 K K p p[t]}{15.+K K p p[t]}$$

$$K p' [t] == \frac{0.025 K[t] K K p[t]}{15.+K[t]} - \frac{0.5 K p[t]}{15.+K p[t]} - \frac{0.025 K K p p[t] K p[t]}{15.+K p[t]} + \frac{0.5 K p p[t]}{15.+K p p[t]}$$

$$K p p' [t] == \frac{0.025 K K p p[t] K p[t]}{15.+K p[t]} - \frac{0.5 K p p[t]}{15.+K p p[t]}$$

Write the model to a file

```
SBMLWrite[inputfile -> "MAPK.xml", outputfile -> "MAPK.html", format -> "HTML"]
```

```
MAPK.html
```