What Values Maximize Activation of Sos?

CMACS - January 2010

Adiba Ishak
Ann Marie Alcocer
Victor Nnah
What Values Maximize Activation of Sos?

- Dimerization Rate
- Ligand-receptor monomers bind to form a dimer

\[ \text{egfr}(l!1,r) + \text{egfr}(l!2,r) \leftrightarrow \text{egfr}(l!1,r!3).\text{egfr}(l!2,r!3) \quad kp2, km2 \]

- \( kp2 \quad 5.556e-6 \)
- \( km2 \quad 0.1 \)
Graph of Active Sos

- Max. Concentration of Active Sos: (9, 13500)
- From $t = 0, 9$; the concentration of Active Sos increases rapidly
- At $t = 50$, the concentration of Active Sos remains constant at a level of 1250
Does Activation of Sos Increase with Dimerization Rates?

- Hypothesis: If we increase the dimerization rate $K_{p2}$, then the concentration of Active Sos will also increase.
Kp2 = 5.556 e-4

- A big increase from the original values (13,500)
Kp2 = 5.556 e-3

- Still increasing

16,440
$Kp2 = 5.556 \times 10^{-2}$

- Not a big increase!
## Summary of Results

<table>
<thead>
<tr>
<th>kp2</th>
<th>Max Concentration of Sos</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.556 e-6</td>
<td>13,500</td>
</tr>
<tr>
<td>5.556 e-4</td>
<td>16,200</td>
</tr>
<tr>
<td>5.556 e-3</td>
<td>16,440</td>
</tr>
<tr>
<td>5.556 e-2</td>
<td>16,490</td>
</tr>
</tbody>
</table>
Parameter Scan of kp2

(.0006, 16272)

Maximum Concentration of Active Sos!
The effect of dimerization rate from $kp_2 = 0$ to $0.0006$

Concentration of Active Sos continues to increase but at a less rapid rate until the increase is insignificant
What about \( km_2 \)?

- \( \text{egfr}(l!1,r) + \text{egfr}(l!2,r) \rightleftharpoons \text{egfr}(l!1,r!3).\text{egfr}(l!2,r!3) \) \( kp_2,km_2 \)

- \( Km_2 \) is the dimer dissociation rate

- How does the reverse rate, \( km_2 \), affect levels of concentration of active Sos? Does decreasing the reverse rate increase the concentration of active Sos?
$km_2 = 0, kp_2 = 5.556 \times 10^{-6}$

The Concentration does increase as $km_2$ is reduced.
\[ km_2 = 0, \ kp_2 = .0006 \]

No increase in Concentration of active Sos when kp2 is at maximum.
Conclusions

• At $t = 9$, the concentration of active Sos reaches a peak and then decreases

• When the dimerization rate is increased, the peak of active Sos also increases

• The concentration only increases greatly until $kp_2 = 0.0006$, after which the increase is insignificant since the slope of the concentration vs. $kp_2$ graph approaches 0

• $km_2$ does not have much of an effect as $kp_2$

• In fact, when $kp_2$ is at 0.0006, reducing $km_2$ has no effect whatsoever
Questions?