Soluble Target at Initial State and Steady State

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1 Some formulas

We will use the notations from *Model F Appendix* in our google drive shared folder.
At initial state, we have

$$\begin{aligned}
\frac{dS_1}{dt} &= 0 \\
\frac{dS_3}{dt} &= 0 \\
M_1 &= M_{10} \\
M_3 &= M_{30} \\
D_1 &= 0 \\
D_3 &= 0 \\
DS_1 &= 0 \\
DS_3 &= 0
\end{aligned}$$

So ODE 13 and 14 give us the following linear system

$$\begin{bmatrix} -(k_{13S} + k_{eS1}) & \frac{V_T}{V_C} k_{31S} \\ \frac{V_C}{V_T} k_{13S} & -(k_{31S} + k_{eS3}) \end{bmatrix} \cdot \begin{bmatrix} S_1 \\ S_3 \end{bmatrix}_0 = \begin{bmatrix} -k_{synS1} - k_{shedM1} M_{10} \\ -k_{synS3} - k_{shedM3} M_{30} \end{bmatrix}$$

So the initial soluble target concentration in the central and tumor compartment is

$$S_{10} = \frac{(k_{31S} + k_{eS3}) \cdot (k_{synS1} + k_{shedM1} M_{10}) + \frac{V_T}{V_C} k_{31S} (k_{synS3} + k_{shedM3} M_{30})}{(k_{13S} + k_{eS1})(k_{31S} + k_{eS3}) - k_{13S} k_{31S}} \tag{1}$$

$$S_{30} = \frac{\frac{V_C}{V_T} \cdot k_{13S} \cdot (k_{synS1} + k_{shedM1} M_{10}) + (k_{13S} + k_{eS1})(k_{synS3} + k_{shedM3} M_{30})}{(k_{13S} + k_{eS1})(k_{31S} + k_{eS3}) - k_{13S} k_{31S}} \tag{2}$$

At steady state, we assume that all soluble target are in the form of bounded complex. By the symmetry of our model, we have

$$S_{1tot,ss} = \frac{(k_{31DS} + k_{eDS3}) \cdot (k_{synS1} + k_{shedDM1} M_{1tot,ss}) + \frac{V_T}{V_C} k_{31DS}(k_{synS3} + k_{shedDM3} M_{3tot,ss})}{(k_{13DS} + k_{eDS1})(k_{31DS} + k_{eDS3}) - k_{13DS} k_{31DS}}$$

$$S_{3tot,ss} = \frac{\frac{V_C}{V_T} k_{13DS} \cdot (k_{synS1} + k_{shedDM1} M_{1tot,ss}) + (k_{13DS} + k_{eDS1})(k_{synS3} + k_{shedDM3} M_{3tot3,ss})}{(k_{13DS} + k_{eDS1})(k_{31DS} + k_{eDS3}) - k_{13DS} k_{31DS}}$$

Formulas for computing membrane target at initial and steady state can be found in *Model F Appendix*, for convenience, I will include them below

$$M_{10} = \frac{(k_{shedM3} + k_{31M} + k_{eM3}) k_{synM1} + \frac{V_T}{V_C} k_{31M} k_{synM3}}{(k_{shedM1} + k_{13M} + k_{eM1})(k_{shedM3} + k_{31M} + k_{eM3}) - k_{13M} k_{31M}}$$

$$M_{30} = \frac{\frac{V_C}{V_T} k_{13M} k_{synM1} + (k_{shedM1} + k_{13M} + k_{eM1}) k_{synM1}}{(k_{shedM1} + k_{13M} + k_{eM1})(k_{shedM3} + k_{31M} + k_{eM3}) - k_{13M} k_{31M}}$$

$$M_{1tot,ss} = \frac{(k_{shedDM3} + k_{31DM} + k_{eDM3}) k_{synM1} + \frac{V_T}{V_C} k_{31DM} k_{synM3}}{(k_{shedDM1} + k_{13DM} + k_{eDM1})(k_{shedDM3} + k_{31DM} + k_{eDM3}) - k_{13DM} k_{31DM}}$$

$$M_{3tot,ss} = \frac{\frac{V_C}{V_T} k_{13DM} k_{synM1} + (k_{shedDM1} + k_{13DM} + k_{eDM1}) k_{synM1}}{(k_{shedDM1} + k_{13DM} + k_{eDM1})(k_{shedDM3} + k_{31DM} + k_{eDM3}) - k_{13DM} k_{31DM}}$$

2 Pseudo-Code for extending the core functions

The formulas to compute various AFIRTS for soluble targets in the tumor compartment are

$$\text{AFIRTS.Kssd} = \text{Kssd.S} \times \frac{\text{Tacc.tum.S}}{\text{B} \times C_{avg1}} \tag{3}$$

$$\text{AFIRTS.Kss} = \text{Kss.S} \times \frac{\text{Tacc.tum.S}}{\text{B} \times C_{avg1}} \tag{4}$$

$$\text{AFIRTS.Kd} = \text{Kd.S} \times \frac{\text{Tacc.tum.S}}{\text{B} \times C_{avg1}} \tag{5}$$

$$\tag{6}$$

Where Kssd.S, Kss.S and Kd.S

$$\text{Kssd.S} = \frac{k_{shedDS3} + k_{31DS} + k_{eDS} + k_{off3}}{k_{on3}} \tag{7}$$

$$\text{Kss.S} = \frac{k_{shedDS3} + k_{eDS} + k_{off3}}{k_{on3}} \tag{8}$$

$$\text{Kd.S} = \frac{k_{off3}}{k_{on3}} \tag{9}$$

$$\tag{10}$$

See Andy's section in Minutes for the derivation. Finally,

$$\text{Tacc.tum.S} = \text{S3tot.ss/S30} \tag{11}$$

To compute AFIRT for soluable target from simulation, do

1. compute Sfree.pct := $\frac{S_3}{S_{30}}$
2. take the average of Sfree.pct in the steady steady state
3. return the result from step 2