SUPPLEMENTARY FIGURE S2

To get an intuitive sense of the competing kinetic processes, we calculated the timescale for each transport step based on the rate constants and physiology in the mouse tumor (**Figure S2A**). Based on the relative magnitude of each step, one can readily appreciate the competing kinetic driving forces that guide the distribution of liposomes and free doxorubicin.

The model can also be used to predict the expected concentrations of doxorubicin in the capillary and interstitial space as well as the quantity that is encapsulated in liposomes, free, located within the cell or bound to DNA. In **Figure S2B**, simulation results for a 3 mg/kg dose of conventional or liposomal doxorubicin show fundamentally different kinetics of DNA-bound doxorubicin within the cell. Administration of free doxorubicin results in quick accumulation of DNA-bound doxorubicin that also quickly washes out. By contrast, liposomal delivery results in a slower accumulation of DNA-bound doxorubicin and a lower peak concentration, but a longer time of exposure. In **Figure S2C**, the corresponding simulations for the human model are shown.

Figure S2A

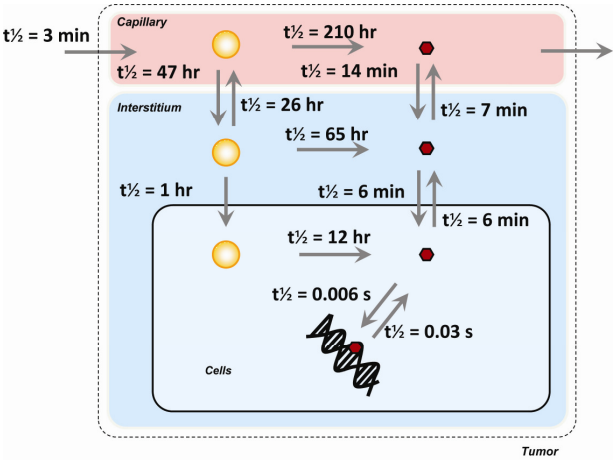
t½ = 3 min
Capillary
t½ = 210 hr
t½ = 47 hr
t½ = 14 min
Interstitium
t½ = 26 hr
t½ = 7 min
t½ = 65 hr
t½ = 1 hr
t½ = 6 min
t½ = 6 min
t½ = 12 hr
t½ = 0.006 s
t½ = 0.03 s
Cells
Tumor

Figure S2B: Mouse Simulation (3 mg/kg doxorubicin or liposomal doxorubicin)

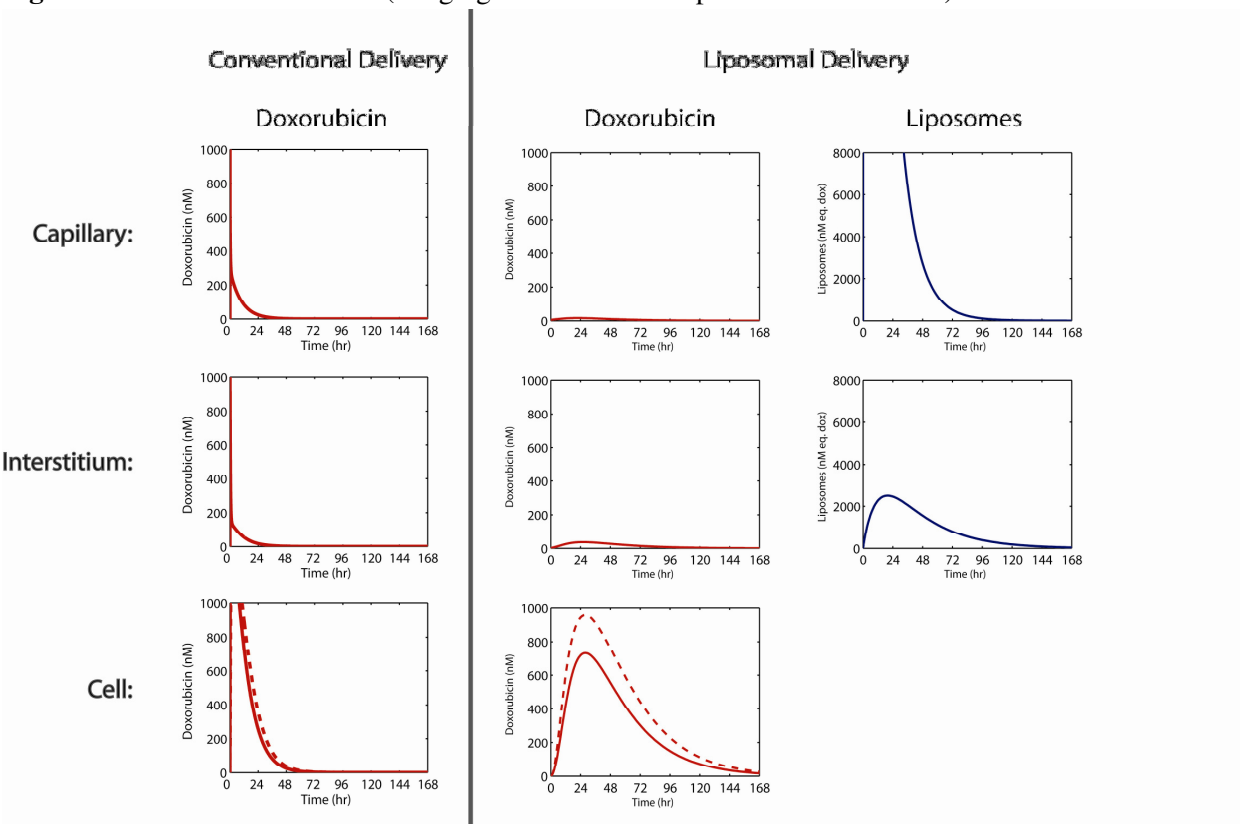

Figure S2C: Human Simulation (40 mg/m^2 doxorubicin or liposomal doxorubicin)