Results for bistable apoptosis model

In this section, a series of simulations have been performed in the case of bistable apoptosis model. With acquirement of either ABC transporter or internal feedback drug resistance, simulation results for bistable apoptosis model display quite similar distribution trends of extracellular, intracellular drug concentration and tumour cell density upon the kinds of stimuli examined here, as shown in Figure S1-Figure S3. Despite the qualitatively different dynamics involved in bistable and monostable apoptosis models, similar conclusions hold good which points to a consistent picture of how a resistance mechanism interacts with an apoptotic pathway which is characterized by threshold and irreversible decision making.

Figure and figure legends

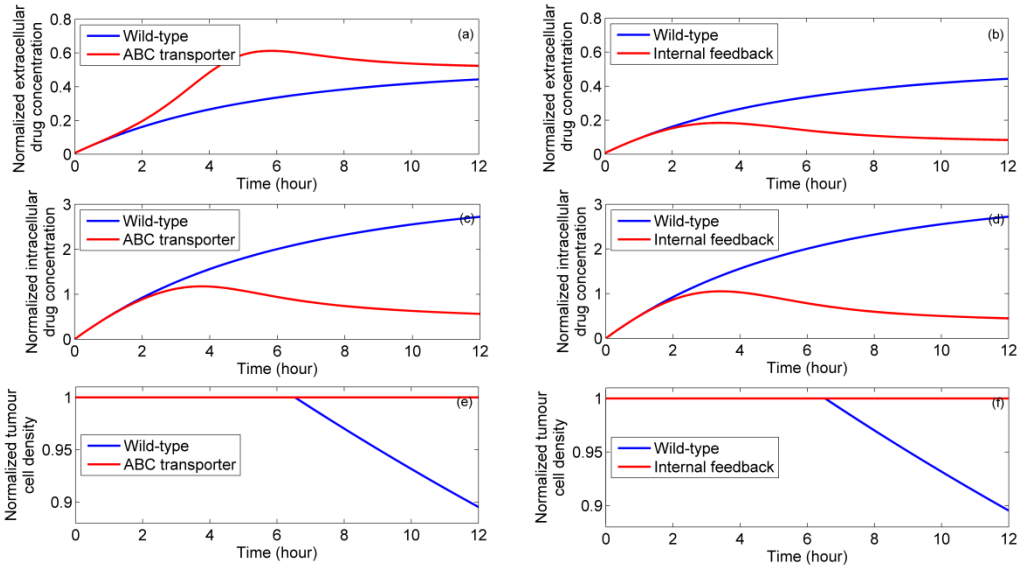

Figure S1: Effect of ABC transporter drug resistance (left column) and internal feedback drug resistance (right column) on temporal profiles of (a) and (b) extracellular drug concentration, (c) and (d) intracellular drug concentration, and (e) and (f) tumour cell density under persistent infusion of drug strength S=2 (in dimensionless terms: see text for details) in the ODE-based model formulation.

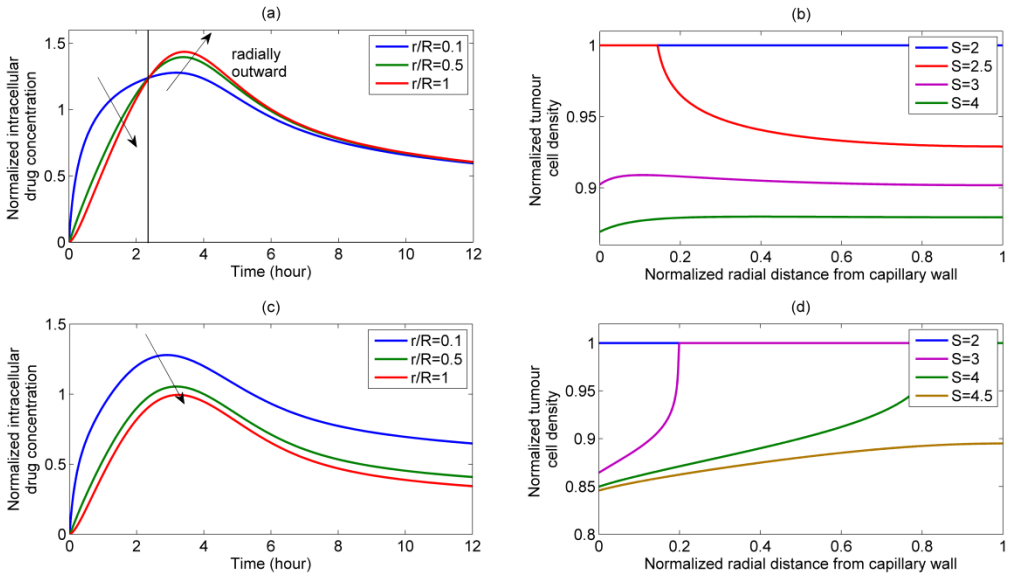

Figure S2: Left column: temporal profiles of intracellular drug concentration at specific spatial locations under persistent infusion, (a) ABC transporter drug resistance at S=2.5, (c) internal feedback drug resistance at S=3; Right column: spatial profiles of tumour cell density at 12h under persistent infusion for varying signal strength, (b) ABC transporter drug resistance, (d) internal feedback drug resistance.

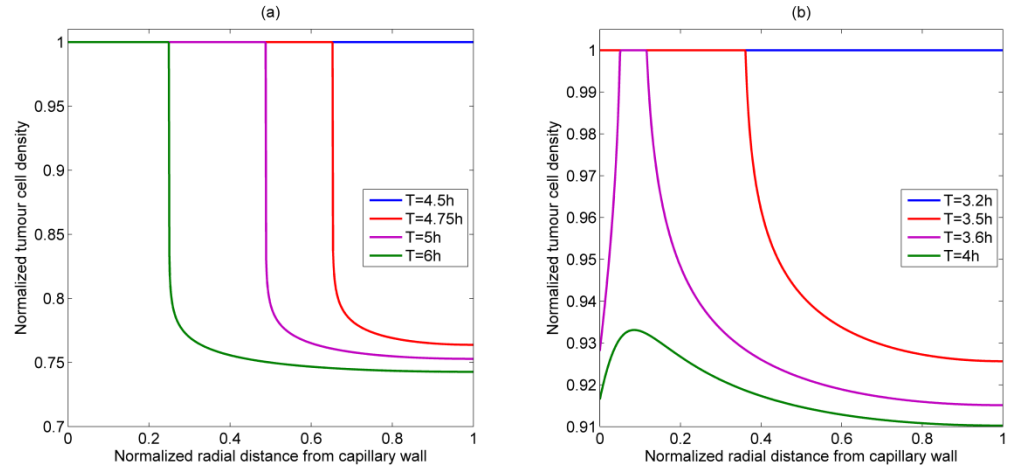

Figure S3: Effects of infusion time on the spatial distribution of tumour cell density at 12h with acquired ABC transporter drug resistance under pulse intensity (a) S=2.5, (b) S=3.