

Overview of the system dynamics resulting from the  $K_{\text{Dcyto}}$  parameter variation

**Supplementary Figure S2**: Tumor dynamics of each defined cell subgroup is shown for different  $K_{D_{cyto}}$  values. In particular, in addition to a considerable amount of surviving sensitive cells S, a reduced cytotoxic drug effect increases the amount of partially-resistant cells  $PR_{aE}$ , first, and fully-resistant cells R, afterwards. A different behavior can be observed for increasing  $K_{D_{cyto}}$  values.

The other parameter values can be found in Supplementary Table S1. A similar administration schedule as that one reported in Supplementary Figure S1 has been considered.