Interrogating and Quantifying In Vitro Cancer Drug Pharmacodynamics via Agent-Based and Bayesian Monte Carlo Modelling

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Supplementary Material

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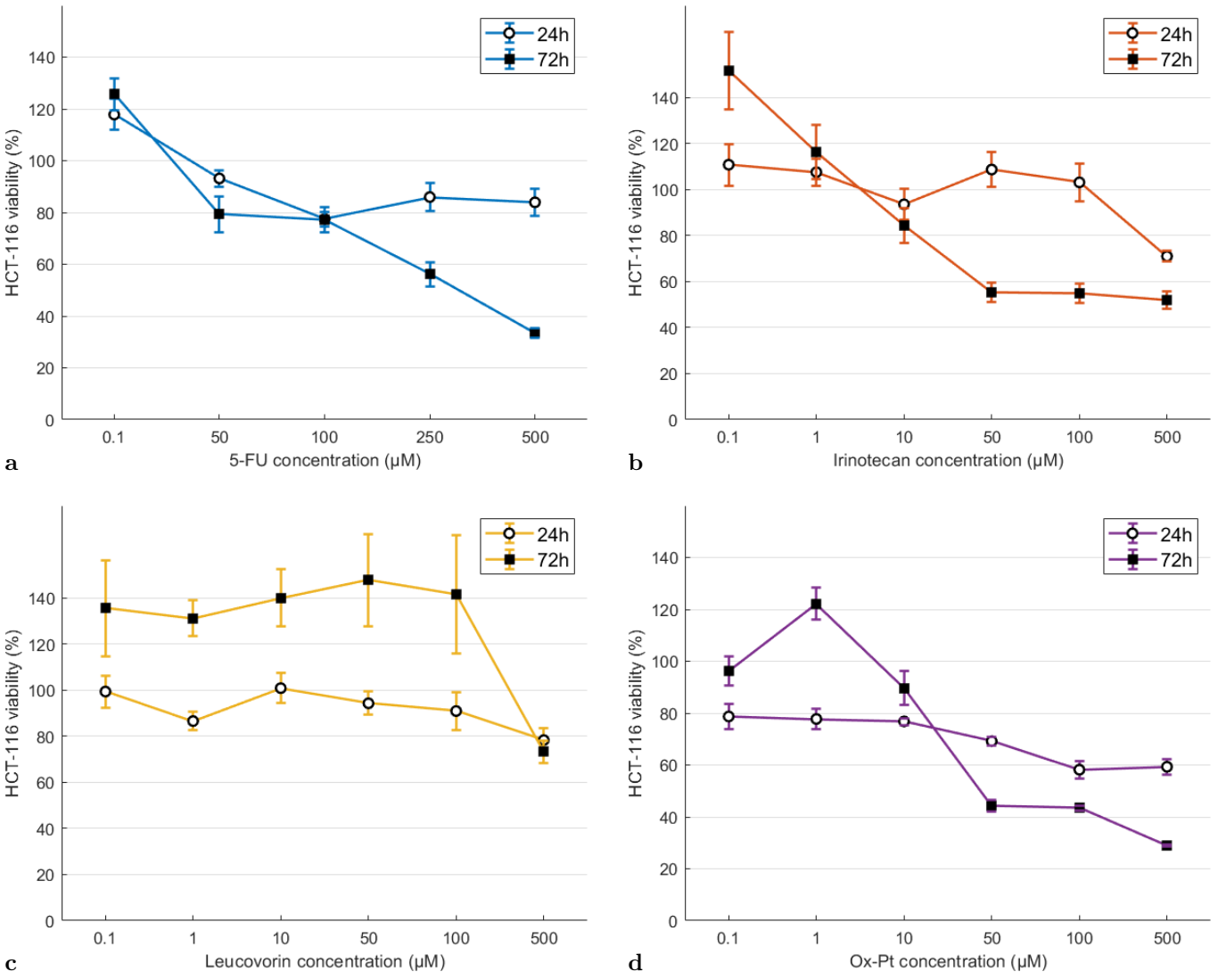


Figure S1: Line plots of the *in vitro* results for the HCT-116 cell line expressed with respect to the drug concentration for every treatment scenario: (**a**) 5-Fluorouracil (5-FU), (**b**) Irinotecan, (**c**) Leucovorin, and (**d**) Oxaliplatin (Ox-Pt) drug. Note, the horizontal axes are not in scale.

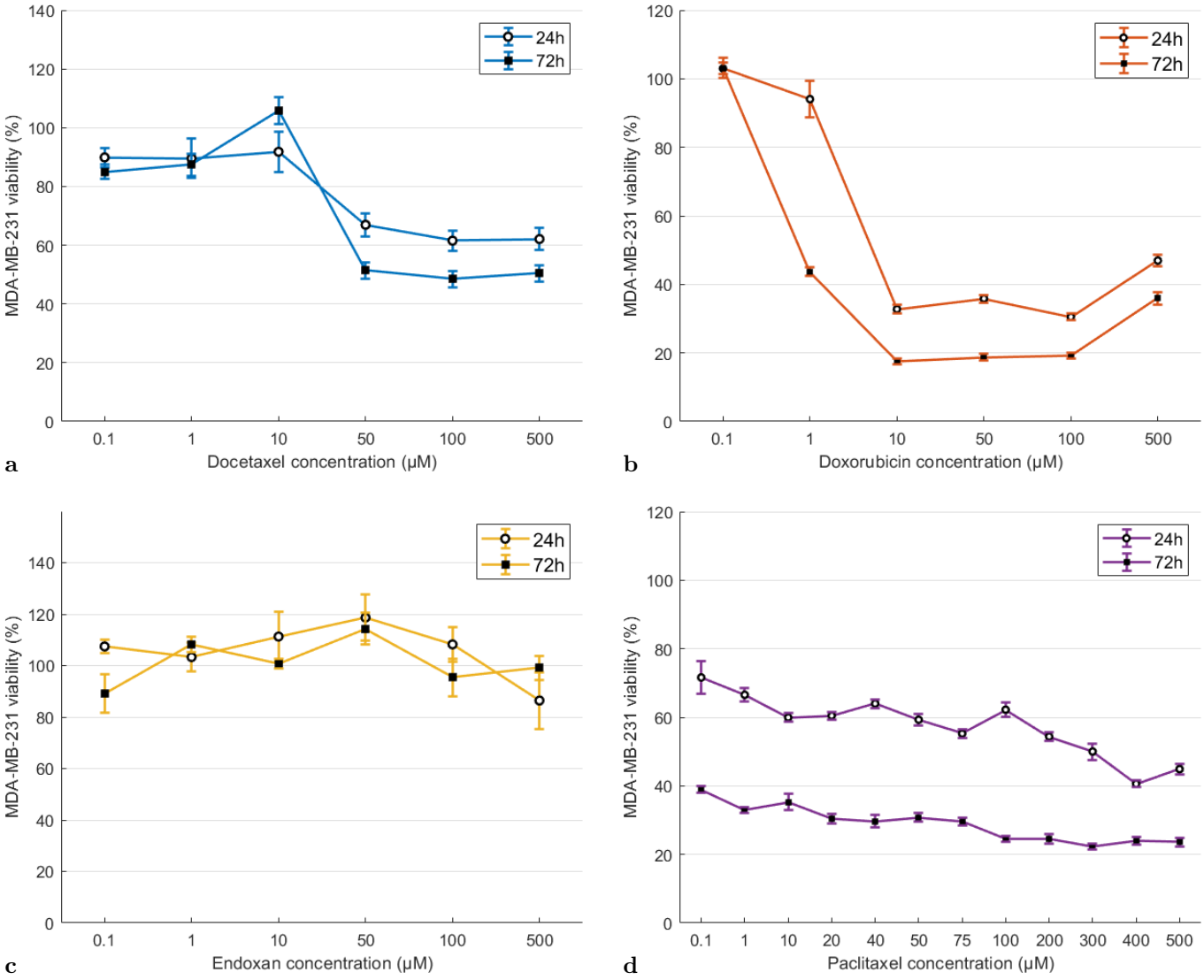


Figure S2: Line plots of the *in vitro* results for the MDA-MB-231 cell line expressed with respect to the drug concentration for every treatment scenario: (**a**) Docetaxel, (**b**) Doxorubicin, (**c**) Endoxan, and (**d**) Paclitaxel drug. Note, the horizontal axes are not in scale.

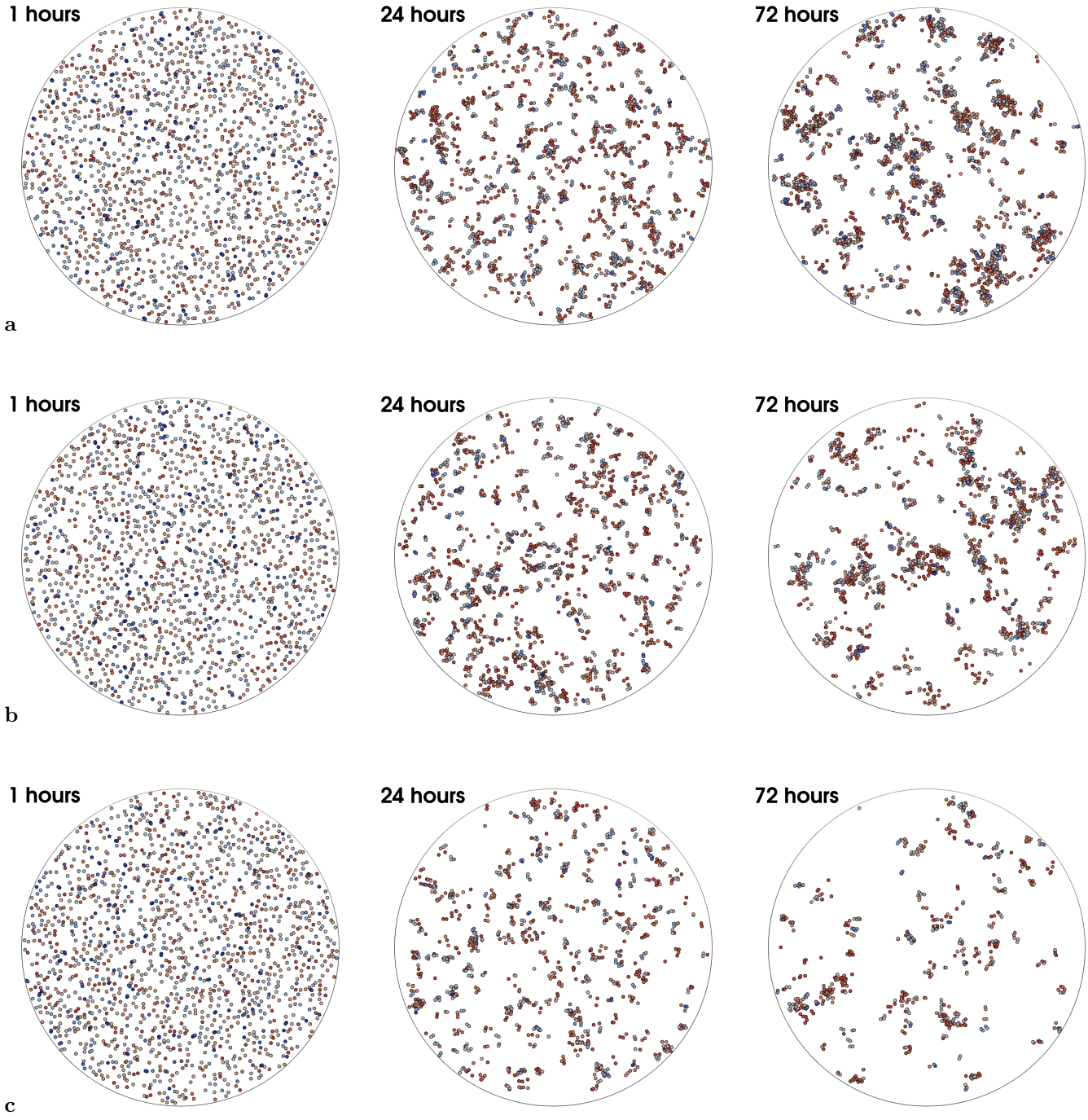


Figure S3: Snapshots of the *in silico* HCT-116 cell population development for the treatment scenario using Irinotecan at drug concentrations (**a**) 0 μM (Control), (**b**) 1 μM, and (**c**) 500 μM, the animations of which can be accessed in Figshare via DOI: 10.6084/m9.figshare.19258799.v1, DOI: 10.6084/m9.figshare.19258811.v1 and DOI: 10.6084/m9.figshare.19258820.v1 respectively.

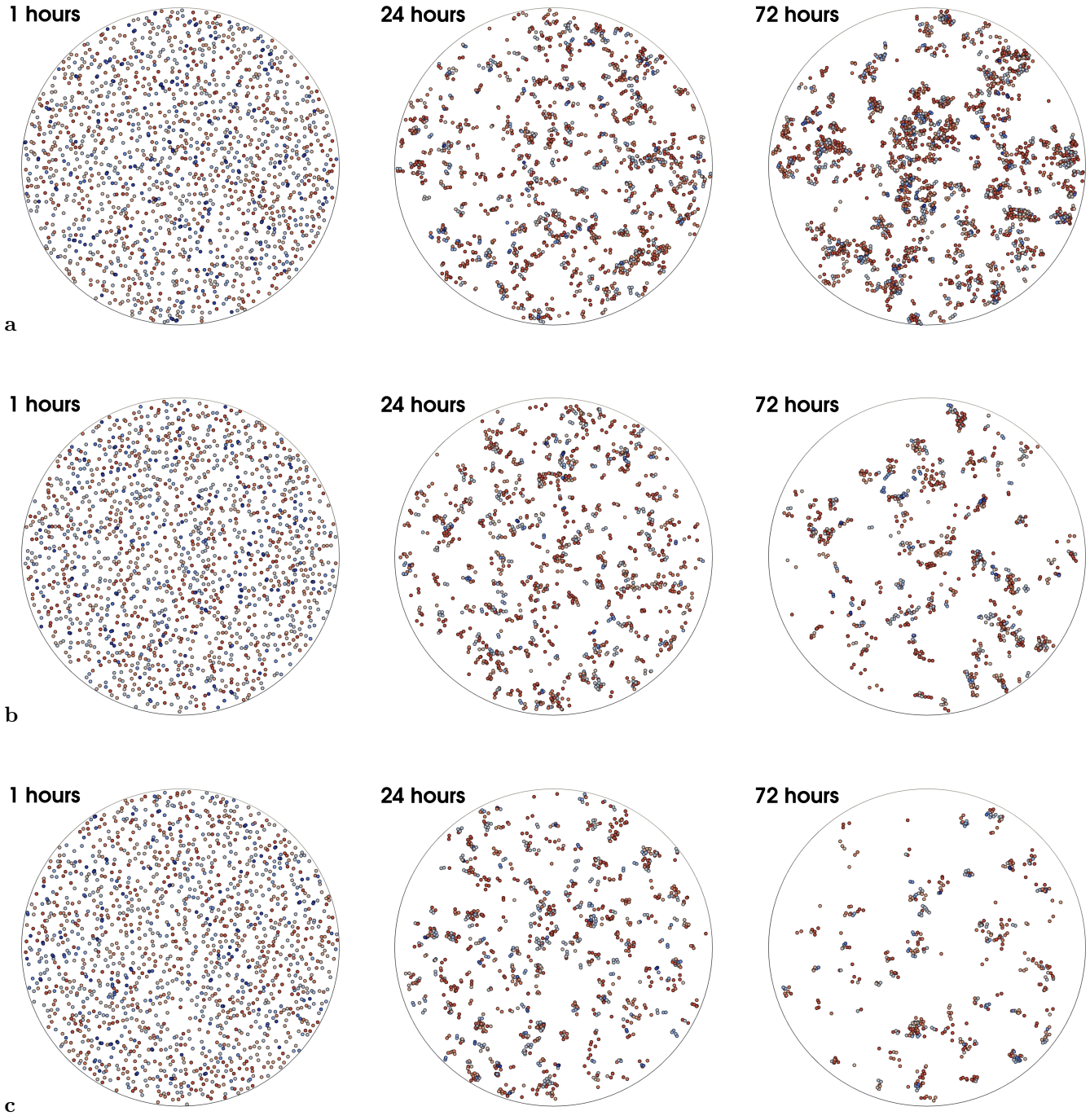


Figure S4: Snapshots of the *in silico* MDA-MB-231 cell population development for the treatment scenario using Paclitaxel at drug concentrations (**a**) 0 μM (Control), (**b**) 1 μM, and (**c**) 500 μM, the animations of which can be accessed in Figshare via DOI:10.6084/m9.figshare.19258826.v1, DOI:10.6084/m9.figshare.19258829.v1 and DOI:10.6084/m9.figshare.19258835.v1 respectively.

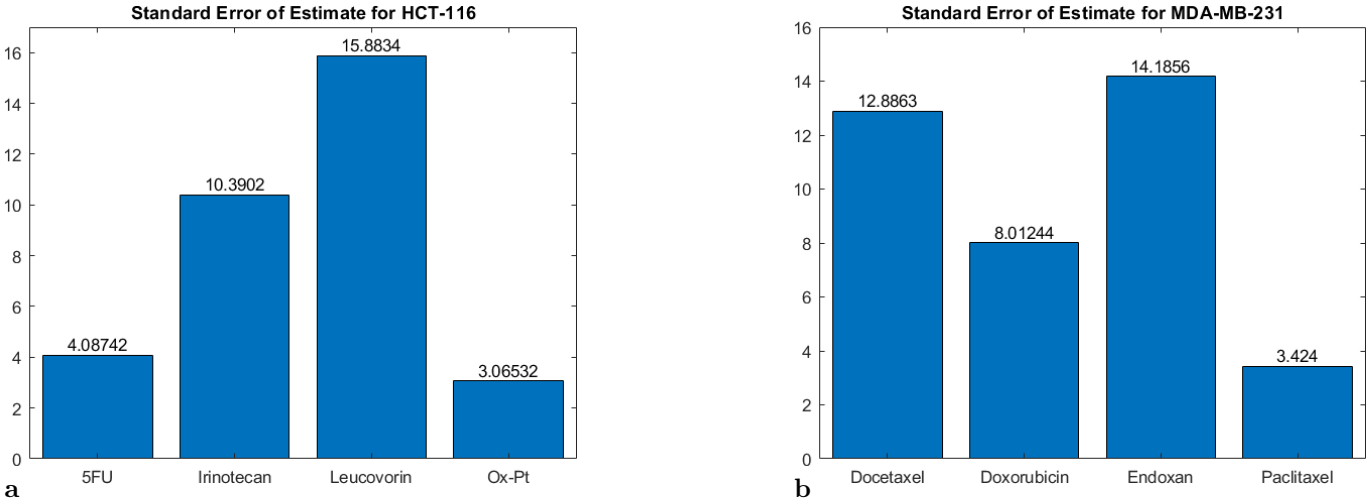


Figure S5: Bar charts of the standard error of the estimate evaluated after linear regression of the *in silico* results against the *in vitro* on the (**a**) HCT-116 and (**b**) MDA-MB-231 cell line respectively.

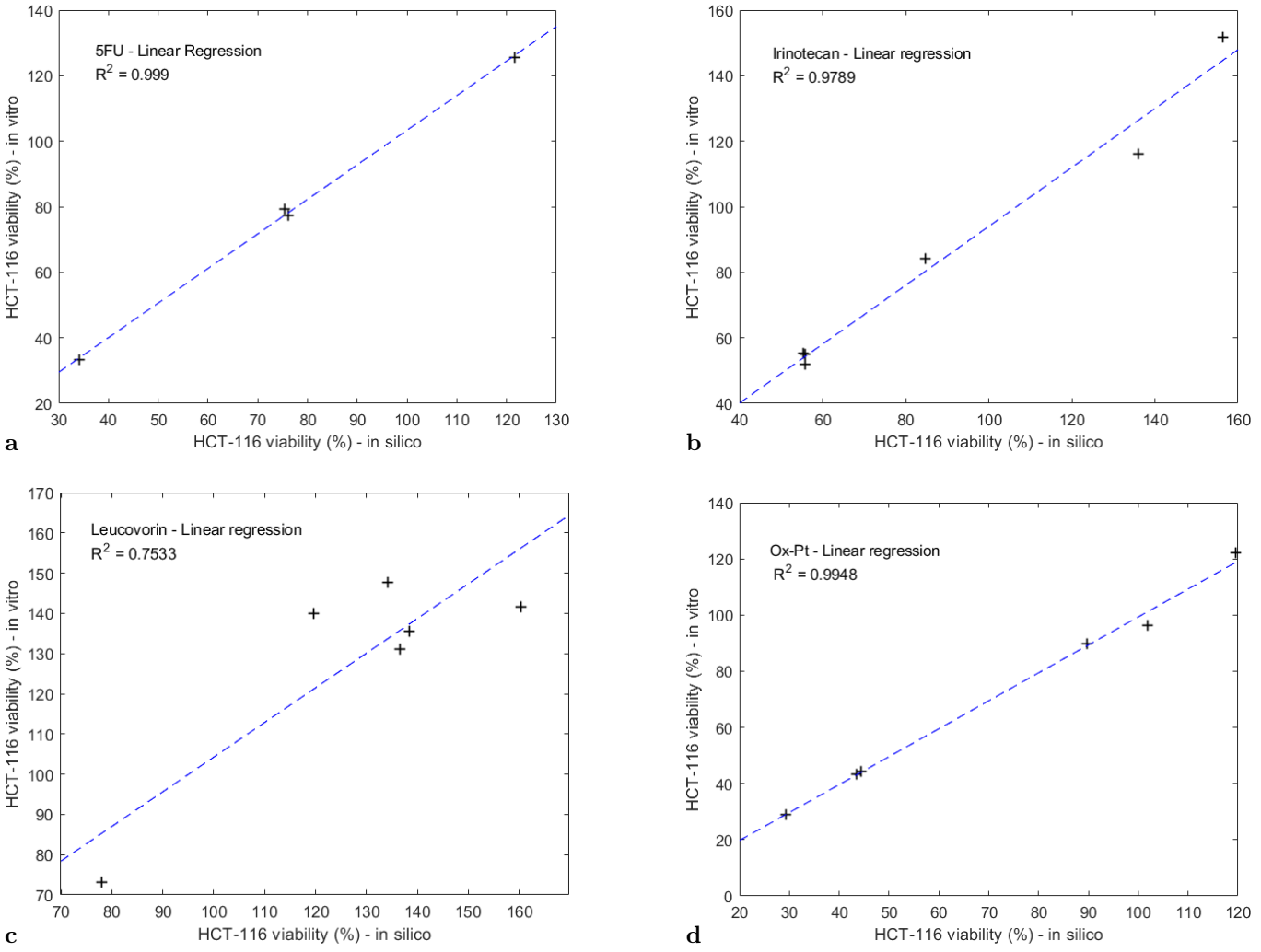


Figure S6: Line plots of the linear regression for HCT-116 cell line viability for the various drug treatment scenarios (*in vitro* versus *in silico* from Figure 3; R^2 values are provided at the legend of each plot).

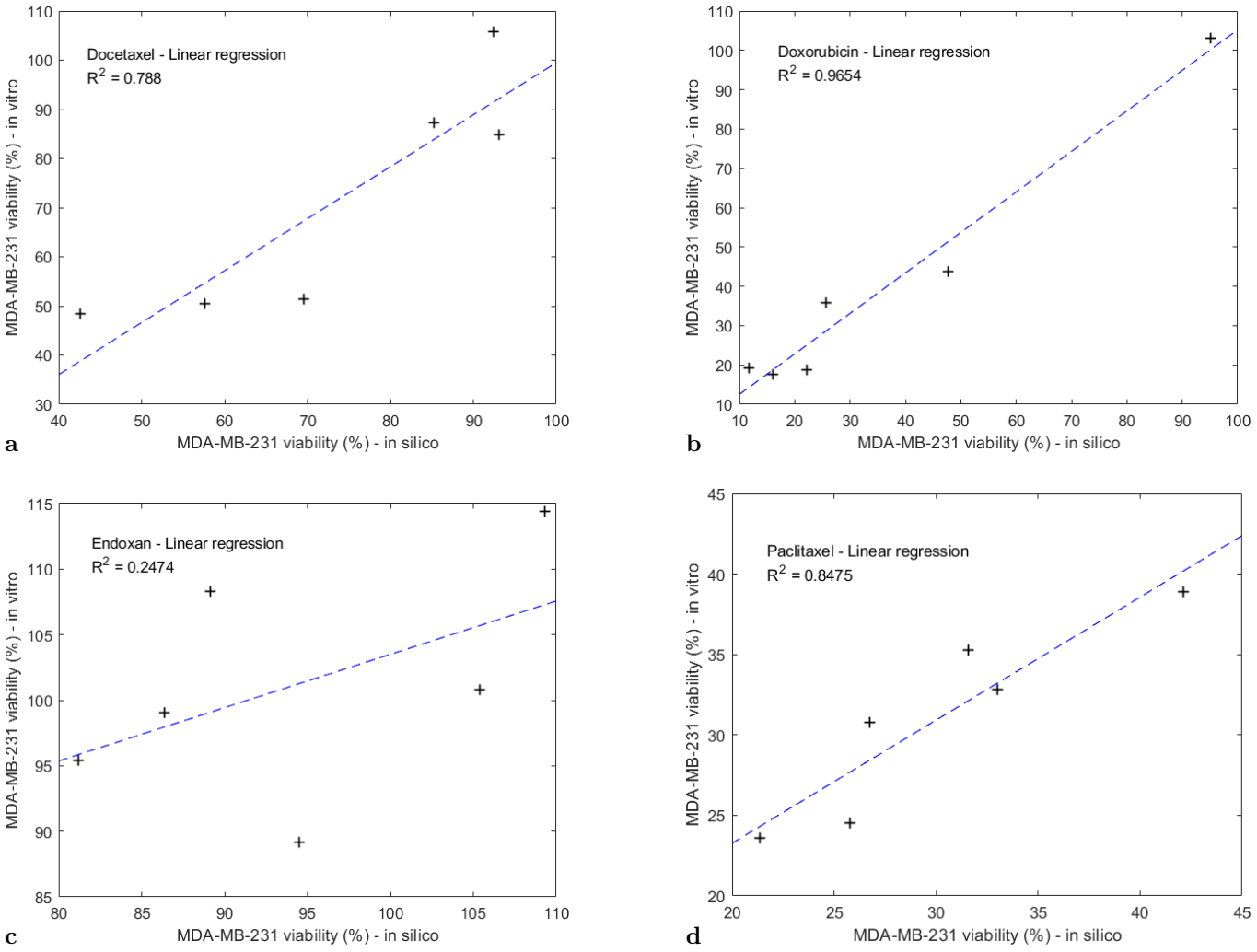


Figure S7: Line plots of the linear regression for MDA-MB-231 cell line viability for the various drug treatment scenarios (*in vitro* versus *in silico* from Figure 4; R^2 values are provided at the legend of each plot).

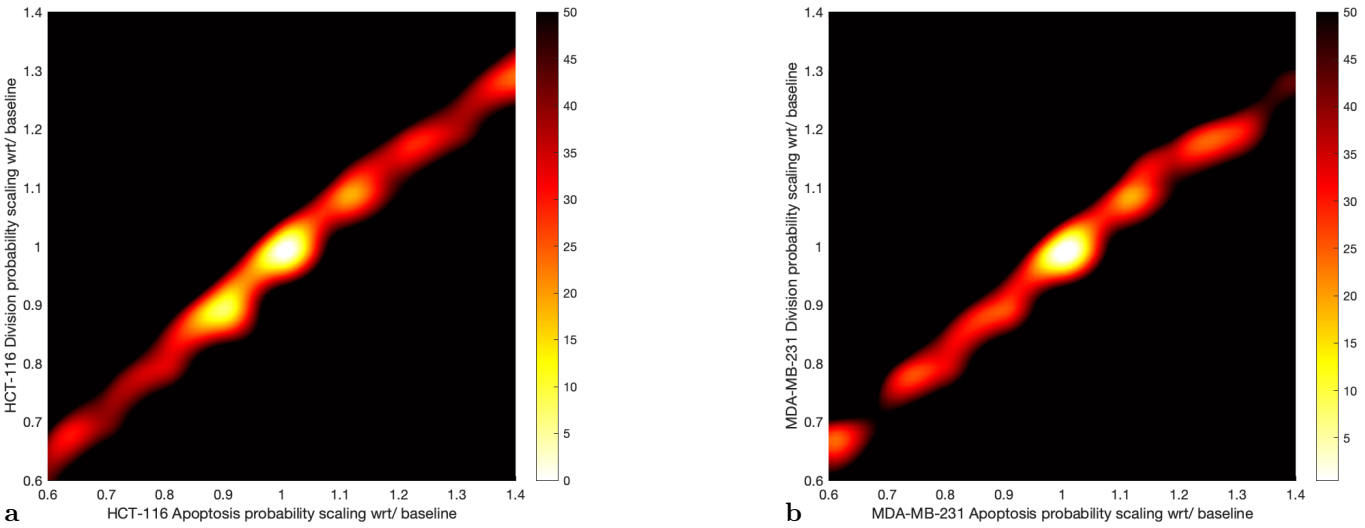


Figure S8: Heat-maps of the absolute error of the simulation results for (**a**) the HCT-116 and (**b**) MDA-MB-231 cell line respectively under control conditions. Horizontal and vertical axis describe the scaling of P_{apoptose} and P_{divide} respectively, with probability parameter values being scaled within a $\pm 40\%$ range with respect to the baseline. The colour-bar represents the percentage of absolute error with black areas corresponding to $\geq 50\%$.

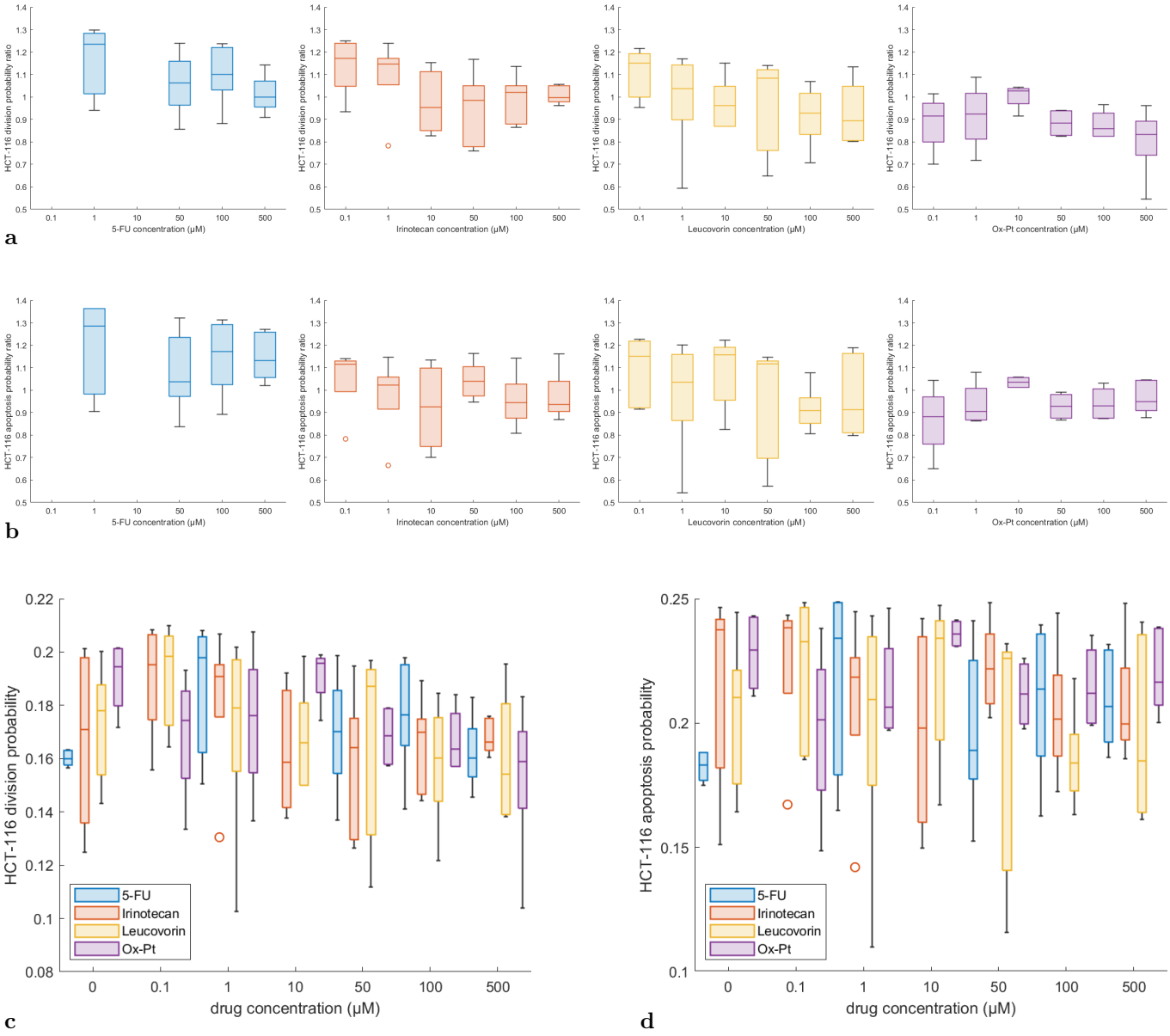


Figure S9: Box plots of the *in silico* model results for the HCT-116 cell line. (**a**) Division probability ratio and (**b**) apoptosis probability ratio simulation results with respect to the drug concentration for every treatment scenario (from left to right: 5-FU, Irinotecan, Leucovorin and Ox-Pt). The box plots of the above simulation results are aggregated with respect to the (**c**) division probability, and (**d**) apoptosis probability versus the drug concentration for every treatment scenario. Zero drug concentration corresponds to the untreated, control, case scenario while the numbers on the drug concentration axis are not in scale.

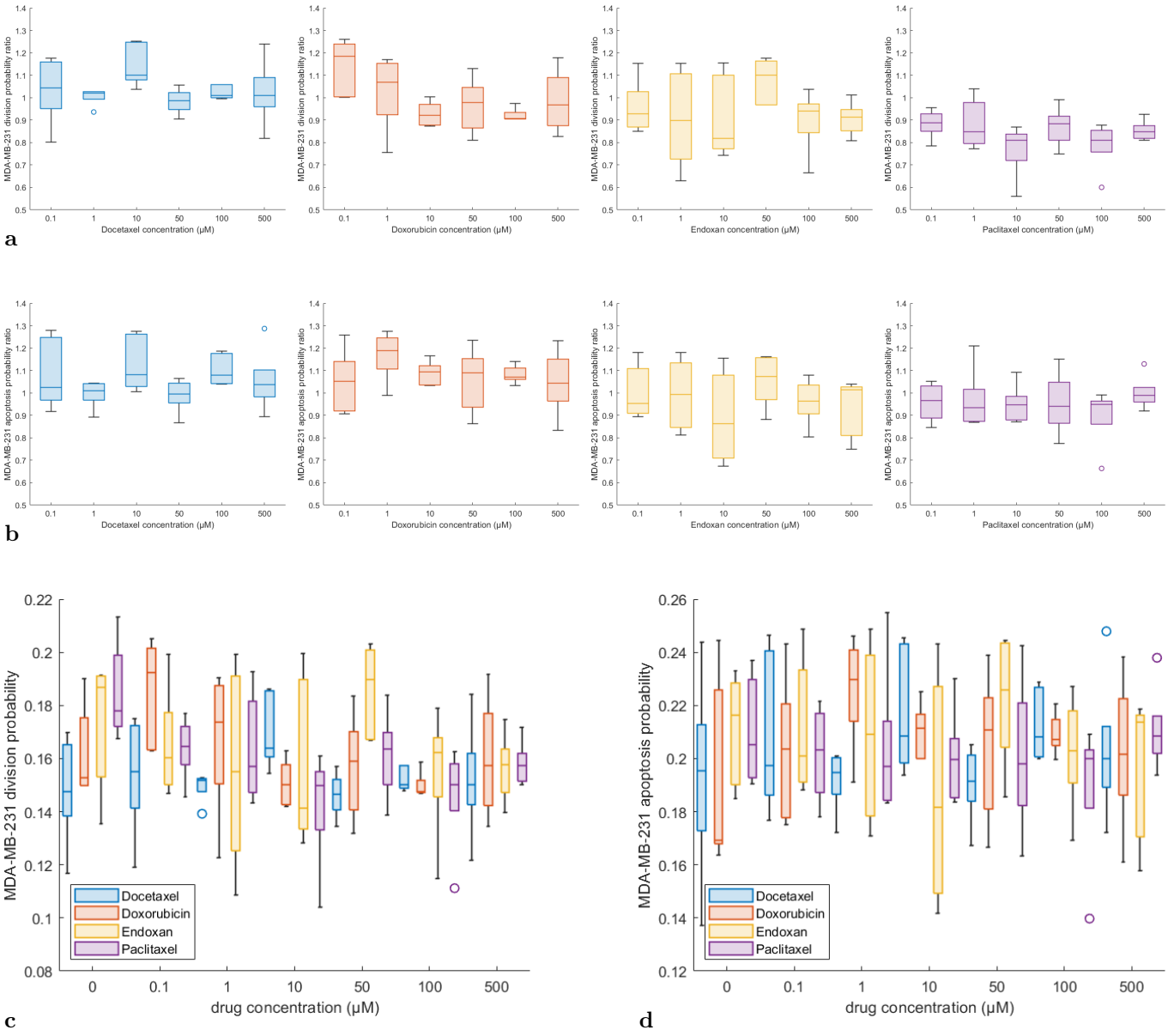


Figure S10: Box plots of the *in silico* model results for the MDA-MB-231 cell line. (**a**) Division probability ratio and (**b**) apoptosis probability ratio simulation results with respect to the drug concentration for every treatment scenario (from left to right: Docetaxel, Doxorubicin, Endoxan and Paclitaxel). The box plots of the above simulation results are aggregated with respect to the (**c**) division probability, and (**d**) apoptosis probability versus the drug concentration for every treatment scenario. Zero drug concentration corresponds to the untreated, control, case scenario while the numbers on the drug concentration axis are not in scale.

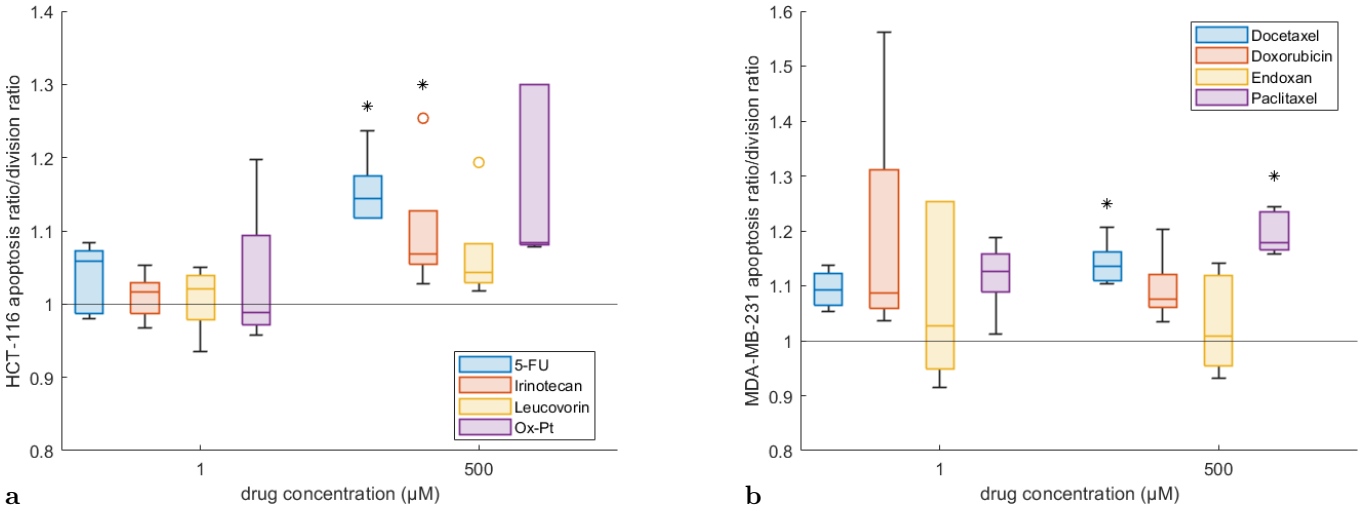


Figure S11: Box plots of the simulation results of the normalised apoptosis probability ratio [$P_{\text{apoptose}}(\textsc{Treated})$ / $P_{\text{apoptose}}(\textsc{Control})$] to the corresponding normalised division probability ratio [$P_{\text{divide}}(\textsc{Treated})$ / $P_{\text{divide}}(\textsc{Control})$] for the (**a**) HCT-116 and (**b**) MDA-MB-231 cell line respectively. Plots include data for every treatment scenario at two extreme drug concentrations. Each scenario is illustrated in a different colour: blue for 5-FU, red for Irinotecan, yellow for Leucovorin, and purple for Ox-Pt drug tested on the HCT-116 cell line; blue for Docetaxel, red for Doxorubicin, yellow for Endoxan, and purple for Paclitaxel drug tested on the MDA-MB-231 cell line. T-tests at 5% significance level are designated with a "*" above corresponding boxes.

5FU concentration (μM)	Apoptosis Probability	Division Probability
0 (Control)	0.18319	0.15984
0.1	0.18694	0.16618
50	0.22001	0.18116
100	0.16258	0.14104
500	0.1861	0.14545
Irinotecan concentration (μM)	Apoptosis Probability	Division Probability
0 (Control)	0.24017	0.2
0.1	0.2406	0.20573
1	0.24473	0.20667
10	0.16341	0.14278
50	0.24852	0.19462
100	0.21099	0.17015
500	0.21099	0.17015
Leucovorin concentration (μM)	Apoptosis Probability	Division Probability
0 (Control)	0.21024	0.178
0.1	0.18531	0.16448
1	0.19664	0.17264
10	0.1702	0.15008
50	0.11598	0.1118
100	0.16322	0.15121
500	0.1612	0.13821
Ox-Pt concentration (μM)	Apoptosis Probability	Division Probability
0 (Control)	0.241664	0.20082
0.1	0.19773	0.1715
1	0.24625	0.20744
10	0.24147	0.19903
50	0.19776	0.1585
100	0.23531	0.18398
500	0.21637	0.16581

Table S1: HCT-116 cell line apoptosis and division probabilities as predicted *in silico* (see Figure 3).

Docetaxel concentration (μM)	Apoptosis Probability	Division Probability
0 (Control)	0.24372	0.14535
0.1	0.17685	0.11921
1	0.1915	0.15267
10	0.19392	0.1543
50	0.16714	0.13441
100	0.2261	0.1575
500	0.19498	0.14958
Doxorubicin concentration (μM)	Apoptosis Probability	Division Probability
0 (Control)	0.24432	0.17047
0.1	0.17513	0.16333
1	0.23892	0.19024
10	0.20002	0.15001
50	0.21077	0.16558
100	0.21077	0.19949
500	0.16098	0.13461
Endoxan concentration (μM)	Apoptosis Probability	Division Probability
0 (Control)	0.191924	0.13556
0.1	0.20088	0.16991
1	0.24864	0.19925
10	0.14178	0.12821
50	0.24337	0.20023
100	0.16935	0.16225
500	0.21369	0.17468
Paclitaxel concentration (μM)	Apoptosis Probability	Division Probability
0 (Control)	0.20536	0.17799
0.1	0.22154	0.17691
1	0.18324	0.14322
10	0.19993	0.15323
50	0.16321	0.13876
100	0.19539	0.15021
500	0.20849	0.15201

Table S2: MDA-MB-231 cell line apoptosis and division probabilities as predicted *in silico* (see Figure 4).

5-FU concentration (μM)	mean (%)	std.(%)
0.1	121.55	3.78
50	75.48	2.23
100	76.06	3.26
500	34.22	1.11
Irinotecan concentration (μM)	mean (%)	std.(%)
0.1	156.38	3.19
1	136.02	2.138
10	84.81	2.595
50	55.43	2.202
100	55.89	2.157
500	55.89	2.157
Leucovorin concentration (μM)	mean (%)	std.(%)
0.1	138.43	3.14
1	136.63	2.44
10	119.60	5.31
50	134.18	2.35
100	160.33	2.98
500	77.95	1.68
Ox-Pt concentration (μM)	mean (%)	std.(%)
0.1	101.80	3.96
1	119.62	3.13
10	89.67	6.63
50	44.33	2.09
100	43.41	0.84
500	29.21	1.27

Table S3: HCT-116 cell line survival percentage as quantified *in silico* (mean and standard error).

Docetaxel concentration (μM)	mean (%)	std.(%)
0.1	93.06	5.41
1	85.29	4.65
10	92.45	2.51
50	69.60	4.71
100	42.60	3.81
500	57.66	3.90
Doxorubicin concentration (μM)	mean (%)	std.(%)
0.1	95.08	27.68
1	47.77	10.72
10	16.10	3.57
50	22.16	8.76
100	11.78	4.93
500	25.61	13.10
Endoxan concentration (μM)	mean (%)	std.(%)
0.1	94.50	0.50
1	89.16	8.00
10	105.36	4.88
50	109.32	12.03
100	81.19	8.03
500	86.36	9.27
Paclitaxel concentration (μM)	mean (%)	std.(%)
0.1	42.11	4.84
1	33.01	4.72
10	31.58	6.83
50	26.73	3.14
100	25.76	2.45
500	21.34	0.48

Table S4: MDA-MB-231 cell line survival percentage as quantified *in silico* (mean and standard error).