A Mathematical Description of Bone Marrow Dynamics of CAR-T Cell Therapy in B-cell Childhood Acute Lymphoblastic Leukemia
Supplementary Information

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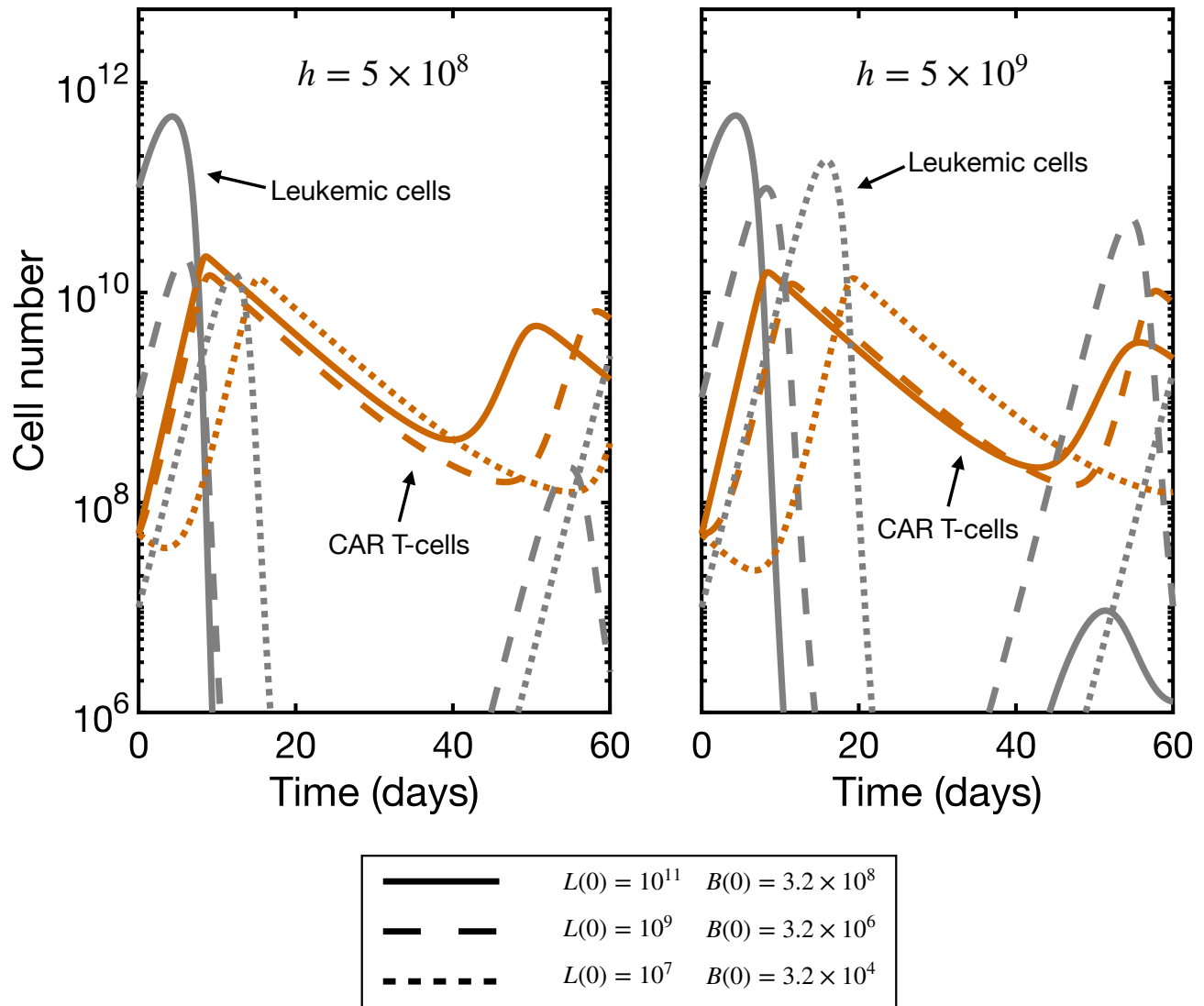
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Figure S1: Influence of low CD19 burden. Evolution in time of leukemic cells (gray) and total CAR T-cells (orange) for different initial configurations (In decreasing order: solid, dashed, dotted lines). Parameters are those of Table 1 with $\alpha = 3 \times 10^{-9}$ day^{-1} · cell^{-1}. In general, leukemia recurrence is more frequent and occurs sooner for higher values of activation threshold and lower CD19 burden.
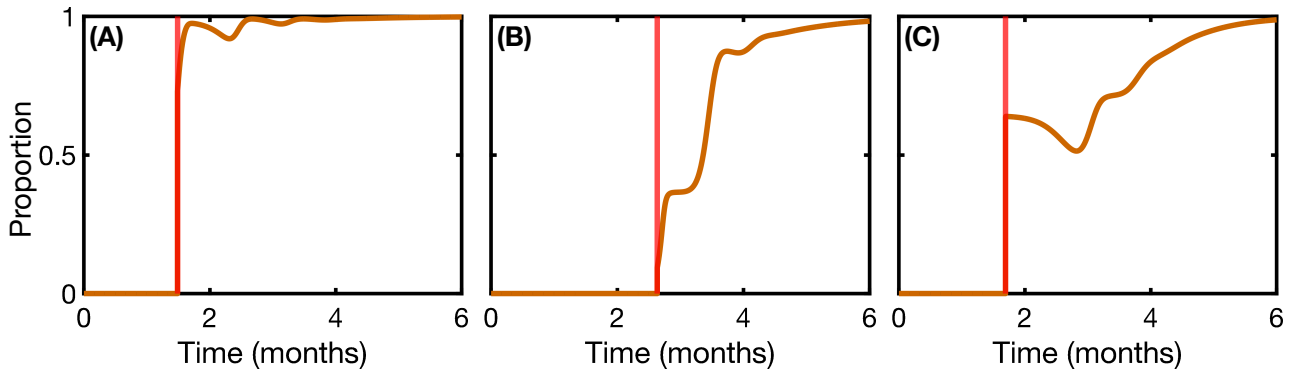
Figure S2: Proportion of newly manufactured CAR after second infusion. Evolution of the proportion of the second CAR infused after lack of response to first infusion, for the case of the improved product. The three cases correspond to the three examples shown in Figure 7, with new attributes (A) $h = 5 \times 10^8$ and $\rho_C = 0.9$, (B) $h = 5 \times 10^8$ and $\alpha = 6 \times 10^{-10}$, (C) $\alpha = 5 \times 10^{-8}$ and $\rho_C = 0.7$. Rest of parameters as in Figure 7.
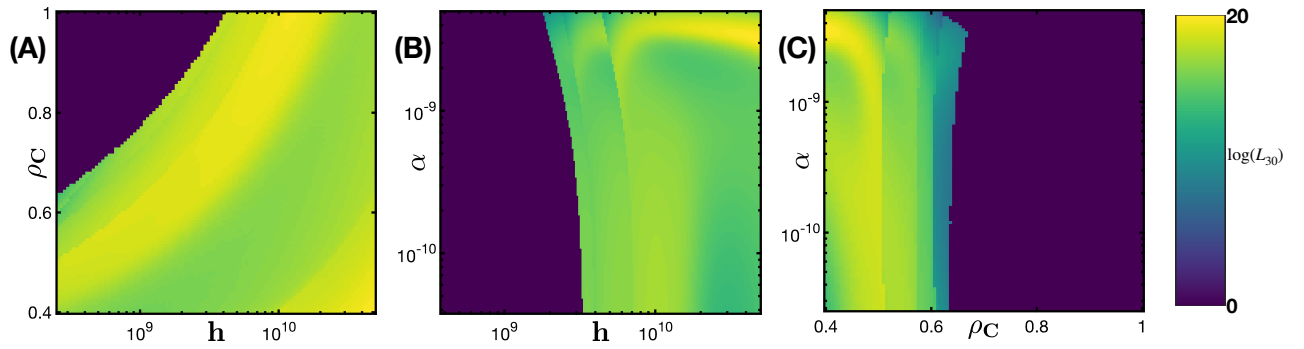
Figure S3: Exploration of parameter ranges for response to second infusion. Number of leukemic cells at day +30 after the second infusion of 5×10^8 CAR T-cells of the initial product, in logarithmic scale. Unchanged parameters and initial state as in Figure 6. Discontinuities correspond to the thresholds (in either cell number or time) set for the moment of reinfusion. Subfigures (A), (B) and (C) correspond to the three heatmaps in Figure 6: Top, middle and bottom respectively.
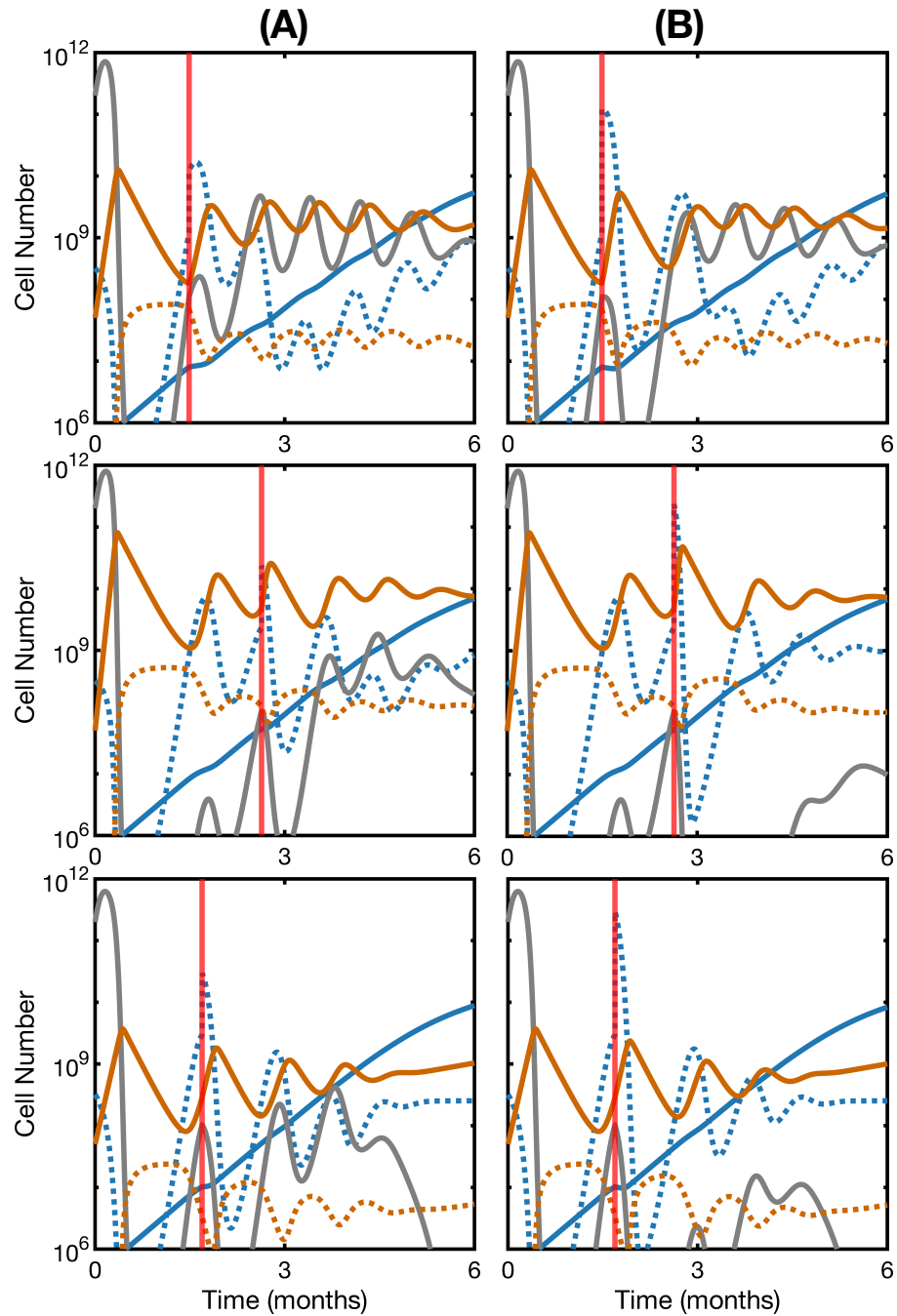
Figure S4: Effect of CD19+ B-cell infusion in non-responding patients. Dynamics of tumor cells (solid gray line), CD19- and CD19+ B-cells (solid and dotted blue lines respectively) and activated and memory CAR T-cells (solid and dotted orange line, respectively), for the three non-responding patients of Figure 6. (A) Infusion of one order of magnitude of CD19+ B-cells at the time of relapse. (B) Infusion of two orders of magnitude of CD19+ B-cells at the time of relapse.