Project 4 – Modeling Antibody Therapy Dynamics in Cancer and other Diseases

(1-26-26)

A brief AI search of this subject uncovered the following 3 references (2016 and 2024), with the paragraphs following presumably extracted from the Abstracts of the first two. They define the problem. All include mechanistic models of the processes described. Enough to get you started.

Frontiers

1. (van Steeg TJ 2016) Design and engineering of bispecific antibodies: insights and practical ...

   Bispecific antibodies (BsAbs) exhibit unique binding kinetics that are crucial for their therapeutic applications. The binding kinetics of BsAbs can be influenced by factors such as the balance between cooperative and competitive binding, the presence of avidity, and the structural complexity of the antibody. Understanding these factors is essential for optimizing the design and engineering of BsAbs to ensure they effectively target their desired targets while minimizing off-target effects.

2. (Ray 2024) Mechanistic computational modeling of monospecific and bispecific ...and
   Cooperative Binding: This occurs when binding to one antigen enhances the binding to the second antigen. It is important to ensure that each binding site retains high affinity for its respective target while maintaining the integrity of the overall structure.

   Competitive Binding: This occurs when binding to one antigen prevents binding to the other. It is crucial to differentiate between these binding behaviors to achieve minimal off-target binding.

   Avidity: Avidity describes the overall binding strength in multivalent interactions, where multiple antibody binding sites contribute to the interaction. It becomes significant when antibodies engage with antigens in a multivalent or complex form.

   The measurement of binding rates and avidity effects in the simultaneous engagement of two antigens by a BsAb is key for understanding and optimizing target selectivity early in the drug development process.

1. (Ng and Bauer 2024) General quasi-equilibrium multivalent binding model to study diverse and complex drug-receptor interactions of biologics

The project

1. Do a more comprehensive literature review of the subject. Must include mechanistic math models. Summarize results of the review and assess the math models found and their similarities and differences with the two refs above.
2. Beginning with the two references above, simulate the models and computational experiments done with them, presumably to analyze the hypotheses presented in the papers about how these mechanisms function in cancer and cancer treatment with Abs. Repeat for other models in references found.
3. **Glofitimab** is a bispecific Ab used in treating lymphoma and possibly other cancers.
   a. How does it fit with any of the models found and implemented?
   b. What parameters of the model correspond to parameters of the model in reference 2, meant to prevent metastasis, to halt tumor growth and/or to kill tumor cells?
   c. Analyze the model further with the goal of reducing side-effects of this Ab drug. Focus on the most common: **Cytokine Release Syndrome (CRS):** Characterized by fever, chills, or difficulty breathing; and **Fatigue:** Feeling very tired or weak.
4. Write a complete report of all your results. It should be prose style, like a paper for publication, and should include: Abstract, Introduction, Methods, Results and Discussion sections. Note: If you get novel results, we can consider publication.

References

Ng, C. M. and R. J. Bauer (2024). "General quasi-equilibrium multivalent binding model to study diverse and complex drug-receptor interactions of biologics." Journal of Pharmacokinetics and Pharmacodynamics **51**(6): 841-857.

Ray, C., Yang, H, Spangler, JB, Gabhann, FM (2024). "Mechanistic computational modeling of monospecific and bispecific antibodies targeting interleukin-6/8 receptors." PLoS Comput Biol **20**(6).

van Steeg TJ, B. K., Dimas N, Sachsenmeier KF, Agoram, B (2016). "The application of mathematical modelling to the design of bispecific monoclonalantibodies." MABS **8**(3): 585-592.