1. What are the main areas of cell- and rule-based applications?

Cell-based and rule-based modeling approaches are commonly used to study multi-cellular biological systems (MCBS). These models simulate the behavior of individual cells, their functions within MCBS, and their interactions with other cells and the environment. Rule-based approaches are often employed in agent-based modeling (ABM), where each cell acts as an independent agent governed by specific rules. Cell-based approaches can also include grid-based methods like cellular automata. Both modeling techniques investigate processes such as cell division, migration, apoptosis, differentiation, proliferation, and tissue organization. Applications include studying angiogenesis, tumor growth, and epithelial morphogenesis.

2. What is the phenomenon of self-metastases shown in Module 4 and its role in tumor migrations?

Self-metastasis refers to the process of self-seeding, in which cancer stem cells migrate away from the primary tumor, seed independent clusters elsewhere, and reappear at the periphery of the primary site. Cells in the tumor core are mostly quiescent, while those at the periphery are more proliferative, contributing to tumor expansion.

3. What is the meaning of quorum sensing in the tumor?

Quorum sensing within tumors serves as a control mechanism that aids a cell in determining whether to differentiate or proliferate based on feedback received from neighboring cells. The distance at which a cell can gather feedback from its neighbors has been identified as the most critical factor influencing the transition from tissue homeostasis to uncontrolled malignant growth (Agur et al 2010).

4. What are the major features of the cell- and rule-based methods?

- Operate on a discrete lattice structure
- Cell or components exist in finite, discrete states ('alive', 'dead')
- Cell behavior depends on the states of neighboring cells within a defined local neighborhood
- Use simple deterministic or stochastic rules for state transition based on local interactions
- In many implementations, all the lattice sites are updated simultaneously at discrete fixed-time steps
- Capture local signaling effects and stochasticity
- Model individual cells or components rather than population-level dynamics
- Suitable for modeling small to medium-scale biological systems
- Can incorporate various cell behaviors such as division, migration, apoptosis, and differentiation
- Can be combined with other biological modeling approaches like continuum models

5. What is the novel treatment discussed in Modules 2 & 3?

The CSC hypothesis suggests that an efficient anticancer treatment should eliminate as many CSCs as possible (cycling and non-cycling), while ''non-stem'' (i.e., differentiated) tumor cells will eventually die out without intervention. To target both cycling and non-cycling CSCs and the total number of cells, optimal cancer treatment must combine differentiation therapy with antiproliferative agents.

6. What are the groups of cells involved in tumor evolution (Module 2 & 3)?

There are two groups of cells involved in the tumor evolution:
- Cancer stem cells (CSCs): they are responsible for tumor growth, relapse, and resistance to therapies and exist in two states:
  - Non-cycling CSCs: that can differentiate into differentiated cancer cells (DCs)
  - Cycling CSCs: that can differentiate into two non-cycling CSCs
- Differentiated Cancer Cells (DCs): these cells have a limited life span and do not live indefinitely. At their death, they create space for CSCs to expand.