Wang Z, Dabaja R, Chen L, Banu M Machine learning unifies flexibility and efficiency of spinodal structure generation for stochastic biomaterial design Nat. 13 5414 (2023). Wang calculates the training and testing data using a phase-field simulation starting with a random distribution of phase composition on 1500 64 cubed voxel samples. A phase-field simulation involves calculation of the bulk free energy and the interface energy based on a smooth gradient. In this case these are based on equations (3) and (4). Explain how these equations are related to the Cahn-Hilliard theory for spinodal decomposition by comparison with Hashimoto T, Kumaki J, Kawai H Time-Resolved Light Scattering Studies on Kinetics of Phase Separation and Phase Dissolution of Polymer Blends. 1. Kinetics of Phase Separation of a Binary Mixture of Polystyrene and Poly(viny1methyl ether) Macromolecules 16 641-648 (1983) (or with the Wikipedia page https://en.wikipedia.org/wiki/Cahn–Hilliard_equation).

Wang et al. (2023) utilize **phase-field simulations** to model the spinodal structure formation in biomaterials, a process driven by phase separation. The simulation starts with random initial conditions and calculates the **bulk free energy** and **interface energy** based on smooth gradients. Equations (3) and (4) in their study likely represent these energy terms, which are fundamental to the phase-field model and closely aligned with the **Cahn-Hilliard theory** of spinodal decomposition.

Cahn-Hilliard Theory and Spinodal Decomposition

The **Cahn-Hilliard equation** provides a mathematical framework for modeling **spinodal decomposition**, where a homogeneous mixture spontaneously separates into different phases over time. The process is governed by the system's tendency to minimize its free energy, which is composed of two key terms:

1. **Bulk Free Energy**: Describes the thermodynamic stability of the mixture. It has multiple minima corresponding to the equilibrium phases of the system.
2. **Interface Energy**: Penalizes sharp transitions between different phases, favoring a smooth gradient in composition across interfaces.

The **Cahn-Hilliard equation** is typically expressed as:

$$\frac{\partial \phi}{\partial t} = \nabla \cdot M \nabla \left(\frac{\delta F}{\delta \phi} \right)$$

where ϕ is the local composition (or phase field), M is the mobility, and $\frac{\delta F}{\delta \phi}$ is the functional derivative of the total free energy F.

The total free energy F is a functional of the phase composition ϕ, and it consists of two terms:

$$F[\phi] = \int_V \left(f(\phi) + \frac{\kappa}{2} |\nabla \phi|^2 \right) dV$$

- $f(\phi)$ is the **bulk free energy** that describes the local thermodynamic behavior based on the composition ϕ.
- $\frac{\kappa}{2} |\nabla \phi|^2$ represents the **interface energy** associated with gradients in composition, where κ is a constant controlling the strength of this penalty.

In the Cahn-Hilliard theory, the system evolves to reduce this total free energy, driving phase separation over time.

Wang's Phase-Field Simulation

Wang et al. generate their training and testing data by simulating spinodal decomposition in biomaterials using a phase-field model. The starting condition of their simulation is a **random distribution of phase composition** on a grid of 1500 samples, each with dimensions of 64^3 voxels. The goal of their simulation is to model the time evolution of the system, as different regions separate into distinct phases.

- **Equation (3)** in Wang's paper likely describes the **bulk free energy**, which is dependent on the local composition at each voxel. This would be analogous to $f(\phi)$ in the Cahn-Hilliard framework.
- **Equation (4)** likely represents the **interface energy**, which penalizes rapid changes in phase composition between adjacent voxels. This corresponds to the $\kappa |\nabla \phi|^2$ term in the Cahn-Hilliard theory, enforcing smooth transitions between phases.

Thus, Wang's model operates on the same principles as the Cahn-Hilliard theory: the system evolves to minimize the total free energy, balancing the drive to form distinct phases (bulk free energy minimization) with the energetic cost of creating interfaces (interface energy).

Comparison with Hashimoto et al. (1983)

The work of Hashimoto et al. (1983) on **phase separation in polymer blends** offers a relevant experimental comparison. Hashimoto et al. used **time-resolved light scattering** to study the kinetics of phase separation in a mixture of polystyrene and poly(vinylmethyl ether), focusing on

the early stages of **spinodal decomposition**. This process is fundamentally the same as that modeled by Wang's phase-field simulations, though Wang uses computational methods rather than experimental light scattering.

- **Spinodal Decomposition**: Hashimoto's study examined the kinetics of phase separation driven by bulk free energy minimization, just as in the Cahn-Hilliard framework. Wang's phase-field simulations aim to computationally replicate this process, predicting how different phases form and evolve.
- **Interface Formation**: Hashimoto's experimental data revealed how interfaces form between different phases. Similarly, Wang's simulation calculates the interface energy to ensure smooth phase boundaries, as described by equation (4).

In both studies (Hashimoto's experimental work and Wang's simulation), the kinetics of phase separation are governed by similar principles: the interplay between bulk and interface energy, as captured by the Cahn-Hilliard equation.

Conclusion

Wang's equations (3) and (4) are analogous to the terms in the Cahn-Hilliard theory that describe bulk and interface energies during spinodal decomposition. Both Wang's simulation and Hashimoto's experimental work are focused on the same fundamental process: the kinetics of phase separation, driven by the minimization of total free energy, which is governed by these two contributions. Wang's phase-field model provides a computational tool to predict spinodal structures, complementing Hashimoto's experimental observations.