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Spatial modelling of Ras protein structures on the cellular membrane

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In cellular signal transduction, it is assumed that spatial effects, e.g., gradients, spatial trends or clustering, play a pivotal role. An example are clusters of the GTPase Ras, a small protein attached to the plasma membrane, which occur in regions measuring up to approximately 20nm in diameter and containing 4 to 10 proteins. Stochastic effects are believed to be of relevance. The cluster size influences the cellular signal transmission, e.g., suppressing the Ras clustering leads to an inhibition of the signal transduction. As mutated Ras proteins have been linked to different human tumours, the cluster structure is of interest for biomedical research.

In this work, spatial effects and stochastic phenomena in context of cellular signal transduction are modelled by a combination of Binomial/Beta, Poisson/Gamma and Dirichlet process mixture models. The spatial dependence of proteins is represented by a nonparametric Dirichlet process mixture of multivariate normals, which infers the intensity surface of the underlying spatial point process. Parameters of the cluster structure are estimated by a Poisson/Gamma model for the cluster size and a Binomial/Beta model for the proportion of clustered proteins.

Results are useful for comparing cells across different experimental conditions, e.g., healthy and tumorous cells.

Keywords:

Spatial point processes; Cluster analysis; Mixture models; Molecular biology.

ABSTRACT
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