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An Improved Non-Affine Arruda-Boyce Type Constitutive Model for Collagen Networks
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This work investigates, by means of computational modeling, the mechanical properties of soft collagen tissues on the basis of elasticity theory.
Bio-polymer networks are structurally disordered and thus compelled to deform non-affine. To capture that in our computational modeling, we supplement the well-known affine Arruda-Boyce model with positional disorder and compute the resultant changes in mechanical response.
We characterize this mechanical behavior as a response to various homogeneous deformations in 3D networks, assuming different constitutive behavior for the individual fibers (in the small deformations linear regime, hookean springs under the entropic elasticity assumption, and in the nonlinear regime freely-jointed and worm-like chains), as well as different coordination numbers (4, 6 or 8 chains connecting at each cross linking point) of the resulting fiber networks. Furthermore we compare the moduli of the simulated networks with their affine deformed counterparts.
Previous work has clearly demonstrated that non-affine deformation modes in elastic (bio)polymer networks greatly affect their mechanics. As the original Arruda-Boyce model can be represented with a particular form of strain-energy function that is micro-mechanically motivated, incorporation of the non-affinity yields amended predictions of the macroscopic mechanical behavior of soft fibrous networks, based on an improved representation of microscopic network structure and deformations. We show that shear and bulk moduli in the Arruda-Boyce model can be as off as 30% when compared with the shear and bulk moduli in the non-affine model.
This entire evaluation of the ways non-affinity enhances the well known Arruda-Boyce model sets the groundwork for developing accurate constitutive relations for fibrous biological materials, for use in finite element analysis of soft tissues.

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Improved Constrained Optimization Method for Reaction-Path Determination in Quantum Mechanical/Molecular Mechanical Calculations
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The nudged elastic band (NEB) and string methods are widely used to obtain the minimum-energy path of chemical reactions and phase transitions. In these methods, however, it is difficult to define an accurate Lagrangian to generate the conservative forces, resulting in slow convergence. On the other hand, the constrained optimization with locally updated planes scheme (CO-LUP) defines the target function properly, although the method does have problems of inaccurate estimation of reactions and inappropriate accumulation of images around the energy minimum. We introduce three modifications into CO-LUP to overcome these problems: (1) An improved tangent estimation of the reaction path, which is used in the NEB method, (2) Redistribution of images using an energy-weighted interpolation before updating local tangents, and (3) Reduction of the number of constraints, in particular translation/rotation constraints, for improved convergence. The present method benefits from a micro-iteration scheme for protein environments in QM/MM optimization. We test the method on the isomerization of alanine dipeptide and found that the method shows 5-8 times faster convergence of the reaction path compared with the NEB or string method using steepest descent. We also apply the method for defining the reaction paths of the rearrangement reaction catalyzed by chorismate mutase (CM), and of the phosphoryl transfer reaction catalyzed by cAMP-dependent protein kinase (PKA). The reaction energy barrier of CM is in high agreement with the experimental value. The path of PKA reveals that the enzyme reaction is associative and there is a late transfer of the substrate proton to Asp166, which is in agreement with the recently published result using the NEB method.

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Cluster Analysis of Protein Point Pattern Sets using Minkowski Functionals
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Point patterns arise in many different areas of physical and applied research, often resulting in sets of patterns that may or may not be fundamenally different. We introduce here a numerical taxonomy procedure for clustering point pattern sets using their approximated Minkowski functionals. We demonstrate that this procedure is robust in distinguishing different spatial processes, even when the number of points in the patterns are small, vary wildly from pattern to pattern, or when the patterns are drawn from very similar processes. We then place this routine in a quantitative biology context by analyzing two point pattern sets of fluorescently labeled inter-cellular proteins, LAT and TAC, that have been acquired from experiments with immune cells. Overall, we find that this routine is a robust method for distinguishing point pattern sets, and provides meaningful insight regarding the homogeneity of a spatial process.

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Simple Stochastic Models for Cell Division
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The experimental measurements show that probability density function for cell generation times in mitosis is non-exponential and goes through the maximum meaning that the rate of cell division depends of the age of cells (the time since theirs birth). The standard Gillespie approach based on the assumption of time independent rate constants is not applicable to model the cell division process. We are aimed to construct the simple model which considers the cell division as a stochastic process. The probability per unit time that a cell undergoes mitosis is time-dependent function that accounts for the typical generation time distributions.
The simulations give results analogous to the solution of the von Foerster equation. In addition, we consider the loss of the cells due to their death which is taken as an age-independent process. The simulations enable to establish the relationship between the average generation times determined from the growth curves for the cell populations and the ones defined by probability density functions. We find how the average net growth rate for the cell populations scales with the different death rates.
We characterize the exponential growth of cell populations by the deviations from the average by the respective dispersions $\sigma 2$ which are found also to grow exponentially with time. However, the relative standard deviation, i.e., the ratio of σ to the average size of population converges quickly to a constant value that depends of the spread of generation time distribution. The more narrow spread of distribution of generation times for the same average generation times yields the smaller variations in sizes for the growing cell populations. The model is generalized for the case that involves the transformation of one type of cells to another in addition to cell reproduction of both types.

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Semi-Automated Image Analysis of Xenopus Laevis Behavioral Response to Visual Stimuli
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High-throughput screens to measure the behavioural effects of various genetic or pharmacological manipulations will require the development of assays that do not rely on subjective human observer input. The Xenopus laevis tadpole is a low-cost, easily accessible vertebrate animal model for studying brain development. We present a new semi-automated image analysis method to quantify avoidance swimming behaviour by multiple tadpoles in parallel. In our setup, Xenopus tadpoles swim in a water-filled Petri dish placed on a computer screen which displays moving dots as escape-evoking visual stimuli on a grey background. Each experiment is recorded by a camera as an image time series. An algorithm was developed to precisely track tadpole movements in space and time. In the control experiments, presenting only the background grey field, we measured the speed distribution of tadpole displacements per image interval. This distribution was used as a reference to assess the tadpole behavioural responses to contrast varying visual stimuli. In experiments where stimuli are brighter or darker with respect to the grey background intensity, we mapped the spatial distribution of responses as a function of the closest dot position with respect to tadpole orientation. We observed a greater response concentration within an area of 5 mm radius around the tadpole. By defining potential reaction events within this threshold minimal distance, we could evaluate the response probability for each tadpole. Our results show a higher tadpole response probability to darker dots than to brighter dots. Furthermore, we show an angular dependence of the response probability that varies with dot contrast. We conclude that this tracking and analysis technique can be applied to a variety of behavioural studies, enabling a rapid and more objective, automated evaluation of visuomotor responses under a wide range of experimental manipulations.