crosslinkers preserved. It is interesting to note that the dissipative and plastic responses of such networks to applied loads are more similar to crack propagation in solids than to standard polymer rheology, where standard mechanisms for energy dissipation are hydrodynamics, filament contour fluctuations, etc. Our results will have important implications for understanding mechanical properties of cytoskeletons, where networks of MTs and Factin bundles crosslinked by different flexible and transient crosslinks are locally deformed by transport of intracellular cargos and by the large-scale structural changes in cell division, motility and morphogenesis.

2828-Plat
Asymmetric Force Response Reveals Mechanical Role in Spindle Protein Localization
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The mitotic spindle is the self-organized, microtubule based structure which mechanically segregates chromosomes during cell division. The spindle 'parts-list' includes microtubules, motor proteins, and non-motor microtubule-associated proteins (or MAPs), and the biochemical properties of many of these components have been well studied. By comparison, our understanding of the force-dependent behavior of many key interactions remains limited. In particular, we do not understand the role that cross-linking MAPs play in providing mechanical stability within the highly dynamic spindle, or how force regulates the function and localization of these proteins. To address this shortcoming, we examine the force-dependent response of NuMA, the major cross-linking MAP of minus-end focused parallel microtubules at the spindle pole. Combining data taken with single molecule TIRF-based imaging and optical trapping methods, we show that NuMA/microtubule interactions generate resistive, friction-like forces which approach ~1pN when dragged at velocities in the micron/sec range. Unexpectedly, the mechanical response is asymmetric, with NuMA sliding more easily towards the minus ends of microtubules than the plus ends. For comparison, we show that PRC1, a dimeric protein which cross-links antiparallel microtubules at the spindle midzone in anaphase, does not possess such an asymmetric behavior under force. We further perform computer simulations on parallel microtubules cross-linked by 'dimerized' NuMA (effectively a minimal structural unit of the spindle pole), and show that in the presence of small oscillatory perturbations, NuMA will migrate to the minus ends. These combined results suggests a mechanism for autonomous localization to the spindle poles, and may reveal a possible mechanical principle underlying spindle self-organization.

2829-Plat
Zipping Dynamics and Turgor Pressure during Dorsal Closure in Early *Drosophila* Development
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Biomechanical processes engaged in morphogenesis require forces to shape multiple tissues in a three-dimensional pattern during metazoan development. Dorsal closure, an essential stage of *Drosophila* embryogenesis, serves as an *in-vivo* model system for cell sheet movements during development and wound healing. During closure two flanks of lateral epidermis approach to close an eye-shaped gap that is initially occupied by a transient amnioserosa tissue in the dorsal opening. Based on a two-dimensional approximation, the time-dependent geometry of the dorsal opening previously has been quantified by four biomechanical processes collectively including apical constriction of amnioserosa cells, tension due to an actomyosin-rich purse string within each leading edge, adhesive zipping at each corner (canthus) of the eye-shaped opening, and resistance due to the lateral epidermis[1]. To more fully understand dorsal closure, we have moved beyond the two-dimensional approximation and report here our three-dimensional investigation. We investigated embryos with GFP/RFP labeled DE-cadherin, myosin, and/or moesin (actin) using time-lapsed confocal microscopy. We observed zipping to be an unexpectedly and remarkably three-dimensional process. The amnioserosa was pushed below the two leading edges of lateral epidermis as they zipped at each canthus. Just prior to zipping, the leading edges slid over the amnioserosa towards the anteroposterior axis. In addition, during early-to-mid stages of closure we observed the amnioserosa in the geometry of a dome. Segmenting this asymmetric dome and fitting with Laplace's formula quantified the turgor pressure. Furthermore, the purse strings that define the dorsal opening were curved in three dimensions with significant bends towards the embryo interior near each canthus. This research has been supported by the NIH, grant No. 33830.
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Platform: Systems Biophysics

2830-Plat
A Model of Nuclear Organization Demonstrates the Effect of Nuclear Envelope - Chromosome Contacts on 3D Organization of Chromosomes
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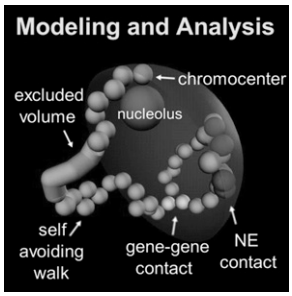
We describe a method for modeling organization of the interphase nucleus, and its application to polytene chromosomes of Drosophila salivary glands. The model represents chromosomes as polymer chains confined within the nucleus. Physical parameters of the model are taken directly from experiment, no fitting parameters are introduced. The model is used to simulate chromosome tracing experiments. When applied to previously published data 33 new chromosome_-nuclear envelope (Chr-NE) contacts are revealed. Most of these new Chr-NE contacts correspond to intercalary heterochromatin - gene poor, dark staining, late replicating regions of the genome; only three correspond to euchromatin - gene rich, light staining, early replicating regions of the genome. Analysis of regions least likely to form Chr-NE contacts reveals that these are mostly euchromatic, but may contain late replication regions or intercalary heterochromatin. We show that Chr-NE contacts may affect long range gene-gene interactions: depending on the chromosome contour length between two contacts, gene-gene interaction probability may increase or decrease. We also develop methods to objectively quantify chromosome territories and intertwining and discuss the corresponding experimental observations.



2831-Plat
Effects of Fluctuation of Chromosome Conformation and Spatial Arrangement of Genes on the Pattern of Gene Expression
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Recently, conformation of all chromosomes in the interphase nucleus of budding yeast has been inferred from the Chromosome Conformation Capture-on-Chip (4C) data (Duan et al., Nature (2010)). However, it has not yet been ascertained how the conformational fluctuation around their mean structures affects the regulation of gene expression. To clarify this issue, we developed a dynamical structural model of interphase chromosomes in budding yeast (Tokuda et al., Biophys. J. (2012)). In the present paper, the effects of the conformational fluctuation and the arrangement of genes on the pattern of gene expression are discussed by using this coarse-grained chromosome model. In particular, the observed difference in the pattern of gene expression between the *yku70 esc1* mutant which abrogates telomere anchoring and the wild-type strain (Taddei et al., Genome Res. (2009)) is studied. In the data of Taddei et al., 32 genes are expressed at higher levels and 28 genes are expressed at lower levels in the *yku70 esc1* mutant than in the wild-type strain. We examine the reason of this misregulation by comparing the fluctuation of the chromosome conformation and spatial arrangement of genes in the case that telomeres are not anchored to the nuclear periphery with that in the anchored case.

2832-Plat
Modeling Stochastic Gene Expression in Growing Cells
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Gene expression is an inherently noisy process. Fluctuations arise at many points in the expression of a gene, as all the salient reactions such as transcription, translation, mRNA degradation etc. are stochastic processes. The flucatuations become important when the cellular copy numbers of the relevant molecules (mRNA or proteins) are low. We investigate different sources of noise in gene expression by considering several models in which protein synthesis and partitioning of proteins during cell dividision are described in either a stochastic or a deterministic way. For regulated genes, a computational complication arises from the fact that protein synthesis rates depend on the concentrations of the transcription factors that regulate the corresponding genes. Because of the growing cell volume, such rates are effectively time-dependent. We deal with the effects of volume growth compuationally using a rather simple method: the growth of the cell volume is incorporated in our simulations by stochastically adding small volume elements to the cell volume.