



# Biological Systems Through the Informational Lens

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## Abstract

Computation is often seen as information processing. Many biological systems may be investigated in terms of information storage, signaling, and data processing networks. Much of this data processing activity is embodied in structural transformations in spatial scales ranging from the molecular to cellular networks. The biomedical sciences make use of an increasingly powerful arsenal of tools and technologies for obtaining structural data as well as details of mass transport and the chemical and electrical signals that underlie these fundamental biological processes. For example, new staining techniques combined with computer-based electron microscope tomography, permit the clear imaging of chromatin filaments in the cell nucleus and filament networks in the cytoplasmic and extracellular space via the electron microscope. The application of tomographic reconstruction software developed at the National Center for Microscopy and Imaging Research (NCMIR) enables detailed 3D reconstructions of the relevant biological structures and processes. In order to deal with fundamental issues related to information processing in biological systems, new data processing methods as well as advances in chemically sensitive probes and imaging technology must be applied across a wide range of spatial and temporal scales. One class of increasingly useful tools for modeling biological systems, evaluating imaging technologies and characterizing the fidelity of digital processing has its roots in theoretical investigations in statistical mechanics, which arise from the concepts of information and entropy. We review how concepts of information and entropy may give new perspectives on the flow of information within biological systems, as well as our instrumentation and computer processing.

*Keywords:* chromatin, perineuronal net, tomography, information theory, Renyi, entropy, radon transform

## 1 Information in structural biology and systems biology

“When the American scientist Claude Shannon found that the mathematical formula of Boltzmann defined a useful quantity in information theory, he hesitated to name this newly discovered quantity

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entropy because of its philosophical baggage. The mathematician John von Neumann encouraged Shannon to go ahead with the name entropy, however, since ‘no one knows what entropy is, so in a debate you will always have the advantage’.” --The American Heritage Book of English Usage, quoted in Borwein Maximum entropy and Feasibility methods for Convex and Nonconvex Inverse Problems.

One answer to this apocryphal anecdote is that information is the change of entropy under transformations of the system under investigation, and that entropy itself can be defined mathematically, in a manner that is consistent with the physics of the system [1].

Recent years have witnessed a remarkable development of technology and tools that support the detailed investigation of biological systems. On one hand, we have the development of fluorescence microscopy [2,3,4,5], which gives highly localized information regarding the activity of protein structures in biological processes. This, on the level of light microscopy, provides a unification of our knowledge of genomics and the metabolic network with our observations of the dynamics of the living cell. On the other hand, with improvements in sample preparation of biological specimens and microscope technology we have been able to extend electron microscope investigations to the resolution of protein assemblies within the cell. Electron tomography (ET) extends these tools to the third dimension [6]. In combination with advanced staining techniques, ET, through imaging contextual structure, can overcome the “pointilist” [1] nature of fluorescence microscopy in the range between 10 to 500 nanometers, provide three dimensional (3D) reconstructions of protein assemblies, correlate 3D structures with functional investigations at the light microscope level and provide structural information which extends the findings of genomics and molecular biology.

One particular area of convergence is between investigations of two of the most information-rich systems known to man--the cell nucleus and nerve cell networks. A central problem in the study of these biological systems is determining how information embodied in the cell nucleus is accessed to control processes in the cell cytoplasm and along the cell membrane. Figure 1, below illustrates biological structures associated with these recently discovered connections. This figure shows sections of 3D tomographic reconstructions made possible, in a large part, by computer software developed at NCMIR.

Figure 1 also illustrates the connection between information in the cell nucleus and information processing in the brain. Recent investigations aimed at long lived proteins, localized by fluorescence microscopy, has pointed toward the hypothesis that networks of long-lived proteins encapsulating neurons, the perineuronal net (PNN) play a determining role in the formation of long-term memory. Findings of a genetic role in abnormalities of the PNN, which lead to development of schizophrenia, have recently attained wide coverage in news media [7,8]. Thus, readout of information of specific genetic information in the DNA, should control changes in brain connection networks and information processing in the brain. The verification of such findings would point toward a detailed and systematic approach to investigation of information transmission within biological systems. Elucidation of the mechanisms of information transfer constitutes an ongoing research problem in biological systems. Beyond this, a systems approach to the issue of information in biological processes may well be extended to the laboratory process as an information transmission system. For example, what information, in the form of entropy, is propagated throughout our experimental procedures? Beyond the conventional techniques of computer based tomographic reconstruction employed by biological researchers, we would propose, as a modest beginning the investigation of entropy measures within the Radon transform and its inversion. Admittedly, the wider biological connections may be tenuous (although tantalizingly promising) at the moment, an examination of our computer processing in terms of entropy and information, has and should continue to contribute new theoretical insights into the mathematics of tomographic reconstruction and lead to new techniques in image processing.

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