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FRACTAL AUDITORY-NERVE FIRING PATTERNS MAY DERIVE FROM FRACTAL SWITCHING IN SENSORY HAIR-CELL ION CHANNELS

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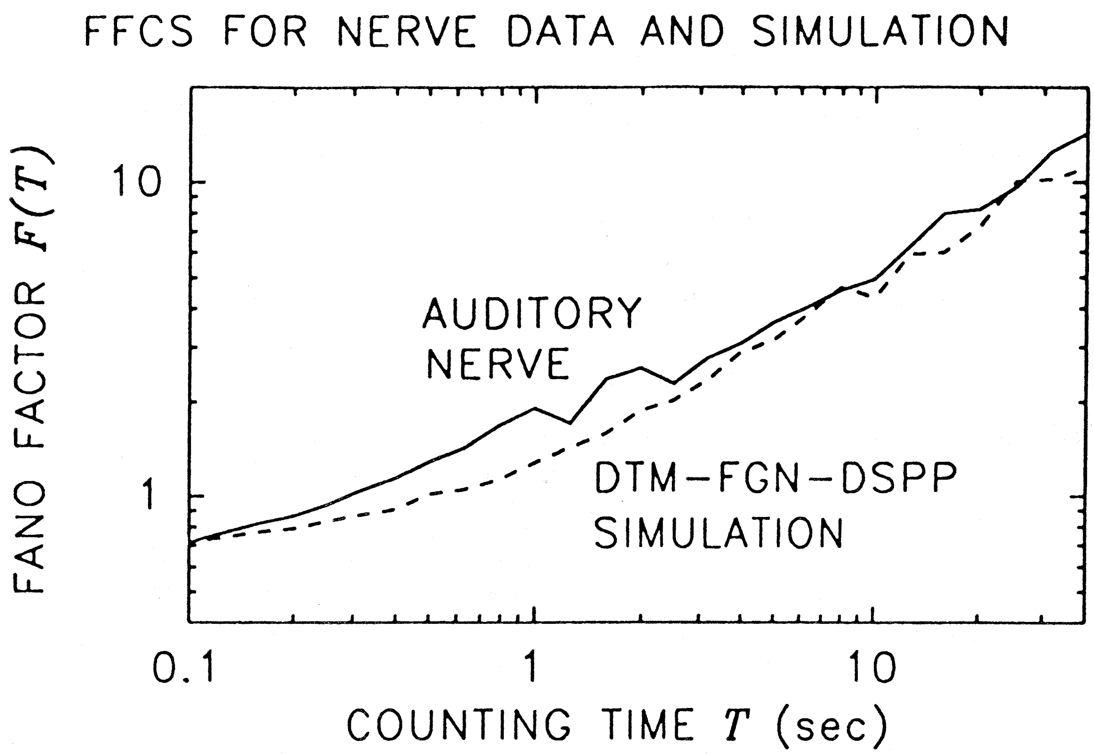
ABSTRACT

Hair-cell ion channels, which provide a crucial link in the transformation of incoming acoustic information to neural action-potential trains, switch between open and closed states with power-law-distributed (fractal) dwell times. Trains of action potentials recorded from auditory nerves in mammals always exibit fractal behavior, including a $1/f$-type spectrum, for long time scales. We provide a mathematical model linking these two fractal behaviors within a common framework.

Transduction of mechanical acoustic information into electrical nerve impulses (action potentials) takes place in the mammalian cochlea. Hair cells in the cochlea release neurotransmitter at a rate which depends on the level of acoustic stimulation; this neurotransmitter, in turn, stimulates action-potential production in primary auditory nerve fibers synapsed to the hair cells. These nerve fibers subsequently transmit this auditory information to the brain. Since the action potentials all have identical waveforms, the information is carried in their relative timing. These action potentials are generated in fractal or clustered patterns even in the absence of external acoustic stimulation.[1–5] Mathematically, the nerve-fiber activity can be modeled as a fractal point process.[6–9]

The statistic that perhaps best illustrates this is the Fano factor $F(T)$, which is defined as the ratio of the variance to the mean number of action potentials counted in a specified counting time T. Varying the counting time T over a range of values generates a Fano-factor time curve (FFC). For a homogeneous Poisson process, the Fano factor assumes a constant value of unity for all counting times T. For short counting times the FFCs computed from auditory-nerve action potentials remain close to unity. However, all auditory-nerve firing patterns examined to date reveal a Fano factor which increases as a power-law function of the counting times, i. e., $F(T) \propto T^{\alpha}$, and this fractal relationship holds for all counting times T between one second and the limit imposed by the finite duration of the recording. The power-law exponent α lies between zero and unity for all such recordings.

In Fig. 1, we present an FFC for the spike train on a cat auditory nerve fiber, recorded in the absence of any stimulation; it shows the typical power-law behavior (solid curve). For this particular recording, $\alpha \approx 0.5$. The power spectral



density of the action-potential point process also follows a power-law form, i. e., $S(f) \propto 1/f^{\alpha}$, with a power-law exponent that has been verified to be identical to the corresponding α from the FFC, both experimentaly and analytically. Other statistical measures, such as rescaled range (R/S), pulse-number distributions (PNDs), and count-based serial correlation coefficients, also highlight the fractal nature of auditory-nerve action potentials, although the FFC presents this information in the most robust manner.

Another statistical measure which yields complementary information, over short time scales, is the interspike-interval histogram, also known as the pulse-interval distribution (PID). The experimental PID exhibits a delayed exponential form. The simplest mathematical model which fits all the above statistical measures for the auditory-nerve firing data appears to be the dead-time-modified fractal-Gaussian-noise-driven doubly stochastic Poisson point process (DTM-FGN-DSPP).[3,5] In this process, fractal Gaussian noise (FGN), with a power spectral density that decays as $1/f^{\alpha}$, serves as the stochastic rate function for a nonhomogeneous Poisson process. The FGN rate function providing the best fit to the data serendipitously has a very small coefficient of variation, ensuring that the rate is almost always positive, thus simplifying the analysis and simulation. Finally, events from this Poisson process which occur within the (nonparalyzable) dead time of a previous event are deleted, resulting in the DTM-FGN-DSPP. Simulations of the DTM-FGN-DSPP [7] yield statistics virtually identical to those of the auditory-nerve data.[3,5] The dotted curve in Fig. 1 shows the FFC for the DTM-FGN-DSPP model, which agrees quite closely with the solid curve generated from the auditory-nerve data.

Might the origin of these fractal action-potential occurrences lie in the fractal activity which also occurs in cochlear hair-cell ion channels? Ion channels switch between two states, open and closed, and the dwell-time distributions often obey power-law forms over a wide range of dwell times.[1,10] Ionic current flows at a constant rate when the channel is open, and not at all when it is closed. Thus a fractal Bernoulli process provides a good model for a single ion channel, and a fractal binomial process models a collection of such channels.[8,9] For independent ion-channel dwell times, the Bernoulli process of the openings and closings of a single channel form an alternating renewal process, and the associated statistics all follow fractal (power-law) forms. For a collection of independent, identical ion channels, the statistics of the resulting binomial process also exhibit fractal behavior. Consider, for example, ion channels with open and closed dwell times $\mathcal{T}$ which have similar fractal distributions decaying as $\Pr\{\mathcal{T} > t\} \propto t^{2-\alpha}$ over some range of dwell times. The resulting fractal Bernoulli and binomial processes have an autocovariance function $C(\tau)$ which decays as $\tau^{\alpha-1}$ and a power spectral density which decays as $1/f^{\alpha}$, where α lies between zero and unity. Furthermore, a power spectral density which decays as $1/f^{\alpha}$, where α again lies between zero and unity, can also be produced when the dwell times in the open state (for example) are negligeable compared to the dwell times in the other state, for which the associated distribution again follows a fractal form, given in this case by $\Pr\{\mathcal{T} > t\} \propto t^{-\alpha}$.

Hair cells contain K^+-ion channels which operate in a fractal fashion, and thus a fractal binomial process is expected to describe the K^+-ion concentration within the cell. This fractal ion-channel behavior is consistent with a fractal alternating renewal process model.[8,9] Since the channels have identical configurations while open, and thus the openings physically resemble a renewal process, for the remaining analysis we make the reasonable assumption that the dwell times within and among channels are independent. Even if such dependency exists, it would likely not affect the predictions of the model.

Since there are many fractal ion channels, as a result of the Central Limit Theorem the binomial process converges to a Gaussian process with the same fractal power spectral density: it is fractal Gaussian noise. Thus the K^+-ion concentration is FGN with an empirical fractal exponent that again lies between zero and unity. Indeed, the voltages of excitable tissue membranes at rest have long been known to exhibit $1/f$-type fluctuations, which have in turn been traced to fluctuating K^+-ion concentrations.[11] This fluctuation establishes the Ca^{++}-ion concentration which, in turn, determines the neurotransmitter secretion that produces a FGN excitation of the auditory nerve fiber proportional to the original FGN K^+-ion concentration. Assuming that an auditory nerve fiber would produce a *homogeneous* Poisson point process in the presence of a steady concentration of neurotransmitter (if it were hypothetically possible to so excite it), then with fluctuations as described above it would generate action potentials as a *doubly stochastic* Poisson point process, with the stochastic rate given by the

FGN-varying neurotransmitter concentration. With the imposition of dead-time effects on the auditory nerve-fiber firings, the resulting process is the DTM-FGN-DSPP.

The approach outlined above is likely to be applicable to a wider range of situations than simply spontaneous auditory nerve-fiber firings. In the presence of a pure-tone stimulus, fractal behavior in the auditory nerve is maintained, but with an apparent increase in the fractal exponent.[2,5] This change presumably originates in a quantitative change in the open- and closed-time distributions for the hair-cell ion channels, but not in a qualitative change from fractal to non-fractal behavior. Finally, inasmuch as fractal ion channels are ubiquitous, similar fractal action-potential activity is likely to appear in other sensory systems, and indeed in many biological systems in general.

The question of the origin of the fractal behavior of the ion channels remains, although several possibilities present themselves. Ion channels are proteins, with a hierarchy of structure on many length scales, and therefore exhibit movement on many time scales. Thus it becomes more convenient to conceptualize ion-channel behavior as $1/f$ noise.[10] Fractal ion-channel behavior then becomes simply a manifestation of the underlying time-scale invariance of the ion-channel protein motion. Another possibility is that the ion-channel fractal behavior is an emergent phenomenon, occurring only in aggregates of intercommunicating channels. Mechanisms for this interaction could range from self-organized criticality, to spatio-temporal chaos, to other cellular automata processes. In that case the channels would no longer be independent, but the overall conclusions would still be valid.

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