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Can the Nyquist-Shannon Theorem be used to Predict when Autophagy fails in order to prevent Brain Disease?

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Abstract:
Millions of people around the world are currently living with neurodegenerative diseases; many of these diseases are caused by the accumulation of misfolded protein (Kopito, 2000). Autophagy acts as the cell's natural cleaning system. However, current biological models are unable to measure exactly when this model fails. This research takes a novel approach to this gap by applying the Nyquist-Shannon Sampling Theorem to cellular proteostasis. Treating autophagic flux as the "sampling frequency" and protein aggregation rate as the "signal", this study proposes a hypothetical "Cellular Speed Limit," and identifies the mathematical cause of cellular failure as "Proteotoxic aliasing," which occurs when the clearance frequency falls below waste accumulation. The resulting model offers a predictive diagnostic framework that detects cellular failure even before clinical symptoms of brain disease appear.

Introduction:

By the time tremors manifest from Parkinson's or memory fades from Alzheimer's, the patient has already lost a significant number of their functioning neurons, reaching up to 60% in specific brain regions (Dauer & Przedborski, 2003). Medicine is currently trapped in a "reactive" loop. It monitors the end stage of the accumulation of misfolded protein without understanding the temporal laws that allowed them to accumulate in the first place. This research suggests that cellular failure is fundamentally an information-processing difficulty that is controlled by the Nyquist-Shannon Sampling Theorem (Shannon, 1948). By viewing the rate of protein aggregation as the "signal" and autophagic flux as the "sampling frequency," disease can be treated as a quantitative calculation rather than a qualitative observation (Mizushima, 2025). If the sampling frequency falls too low, an audio recording becomes distorted due to aliasing. Correspondingly, a neuron will face "proteotoxic aliasing" if its cleaning rate is unable to keep up with protein damage. Through this interplay between Information Theory and Cellular Biology, this study aims to establish a "Cellular Speed Limit" that serves as a quantitative biomarker. It provides a mathematical threshold for detecting sub-cellular failure, thereby revolutionizing diagnostic processes and allowing for intervention before irreversible damage can occur.

Literature review:
Current research on proteostasis has successfully identified the molecular regulators of autophagy (He & Klionsky, 2009). Still, we cannot predict exactly when these systems will fail. Recent work by Koh et al. (2019) found that the lysosome experiences a physical bottleneck. This then proves that the processing of cellular waste falls under a certain "ceiling." Survival relies on autophagy, but also on when and how often the cell samples its environment. Levchenko, A., & Madsen, R. R. (2026) support this as we establish that cells recognize waste via discrete signaling pulses through their research. This mechanism provides a biological "sampling frequency".

The challenge is that protein aggregation does not occur at a steady rate. Instead, it arrives in sudden, high-speed bursts (Kopito, 2000), causing significant cellular noise. We need to determine the proteostatic "red line", where the clearance rate can no longer keep up with cellular damage (Hipp et al., 2019). This study moves past describing biology and starts calculating it. It utilises the Shannon-Nyquist Theorem (Shannon, 1948) to calculate the speed limit for neuron survival, enabling the prediction of autophagy failure to aid in the prevention of brain disease.

Methodology:

This study will simulate cellular autophagic clearance using a discrete digital sampling system. The periodic protein aggregation will be represented by a continuous signal, $x(t)$. The framework, shown in Figure 1, follows a block-diagram workflow. It tracks the signal from the protein's production to its reconstruction in the lysosome. To establish the exact clearance rate necessary for homeostasis, a Fourier Transform simulation will be used to analyse the "bandwidth" (B) of the protein bursts (Bracewell, 1986). This will determine the Nyquist Limit (2B) as the model's critical threshold (Shannon, 1948). This mathematical constraint dictates that the autophagic flux (f_s) must be at least twice the frequency of protein production. This balance helps avoid system failure.

The simulation will be developed in a Python 3.12 environment using the NumPy library for mathematical operations and Matplotlib for data visualization (Harris et al., 2020). These tools will help create a precise iteration loop representing a 100-year cellular lifespan. To test the core theory, Figure 2 will provide a comparison of the two cellular states. Panel A will depict a healthy neuron where sampling will be at a high frequency to capture every peak of the protein signal. In Panel B, we will lower the frequency to find the start of "Proteotoxic Aliasing." This occurs when the cell fails to recognise and eliminate high-speed waste bursts. A decay function will be incorporated into the code to decrease the autophagic efficiency by a steady 0.8% each iteration. This change will simulate biological aging. This measure is modeled after the age-related decline in lysosomal efficiency observed in biogerontology (Cuervo & Dice, 2000). Though natural aging is often unpredictable, this model uses a linear decay as a control variable. This will ensure that any sudden protein spike comes from crossing the Nyquist Limit, not from an abrupt change in aging speed. This model will examine whether a gradual decline in autophagic efficiency can lead to sudden system failure when the Nyquist Limit is crossed.

Figure 3 provides the primary evidence of the research. The simulation will observe how declining autophagic efficiency relates to the fixed safety threshold. The cell is expected to remain stable above the threshold for about 75% of the timeline, and the system will be set to identify the specific intersection, referred to as the "Red Line." This is where the clearance rate drops below the required bandwidth. At the "Red Line," protein accumulation is predicted to spike exponentially, aligning with the rapid clinical decline seen in neurodegeneration.

Because computer models are simplified, assumptions such as signal periodicity and the linearity of cellular aging must be made. These limitations will be accounted for by cross-validating the signal's "failure age" with clinical data on neuron loss (Hipp et al., 2019). This methodology will demonstrate how applying Information Theory principles to biogerontology can provide a quantitative, predictive model for understanding the critical thresholds in age-related diseases.

Conclusion:

The study defines "proteotoxic aliasing" and proves that neuron survival can be measured quantitatively. While the current linear model of biological age serves as a necessary idealized simulation, the principle of this framework can be expanded to include stochastic biological variables. The "red line" establishes a foundation for predictive and proactive diagnostics, facilitating clinical intervention before any irreversible damage occurs.

Figure 1: Flowchart of the Nyquist-Shannon Autophagy Model

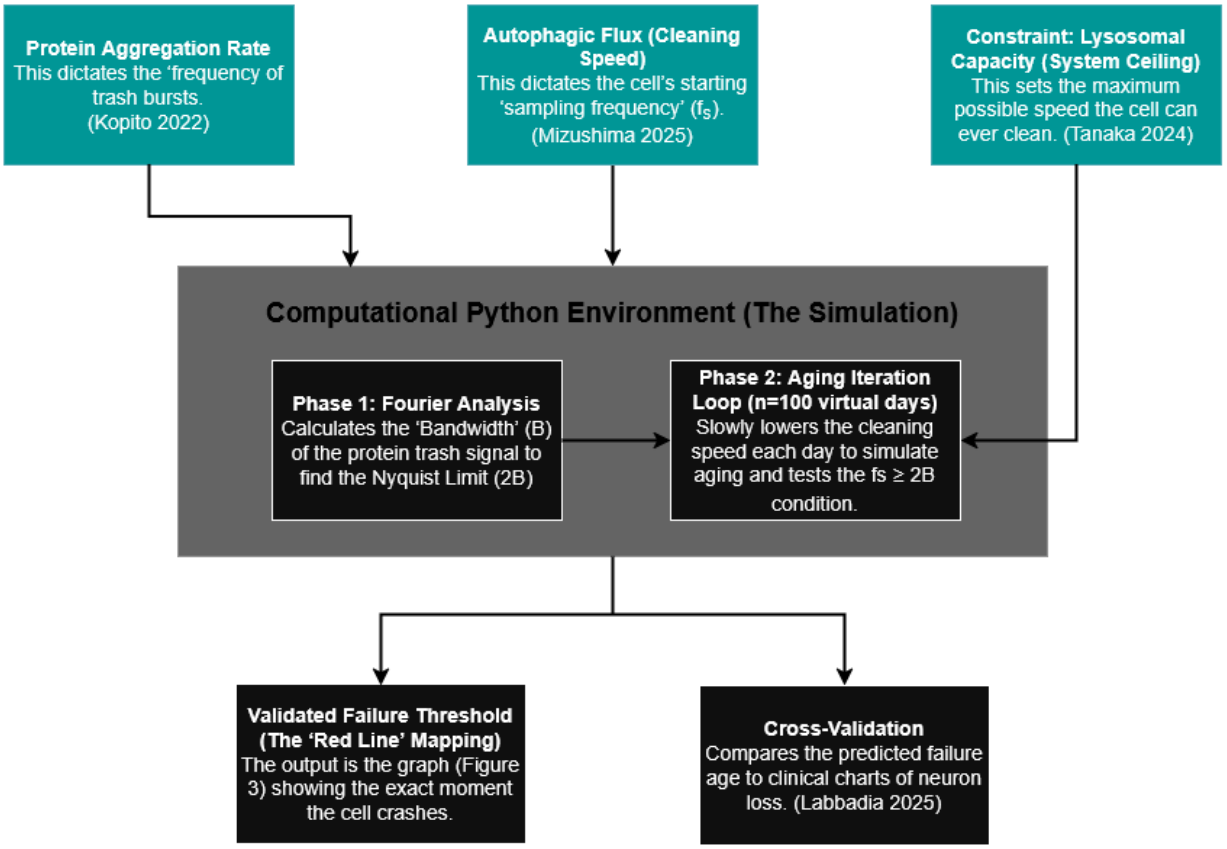


Figure 2: Comparative Analysis of Proteostatic States

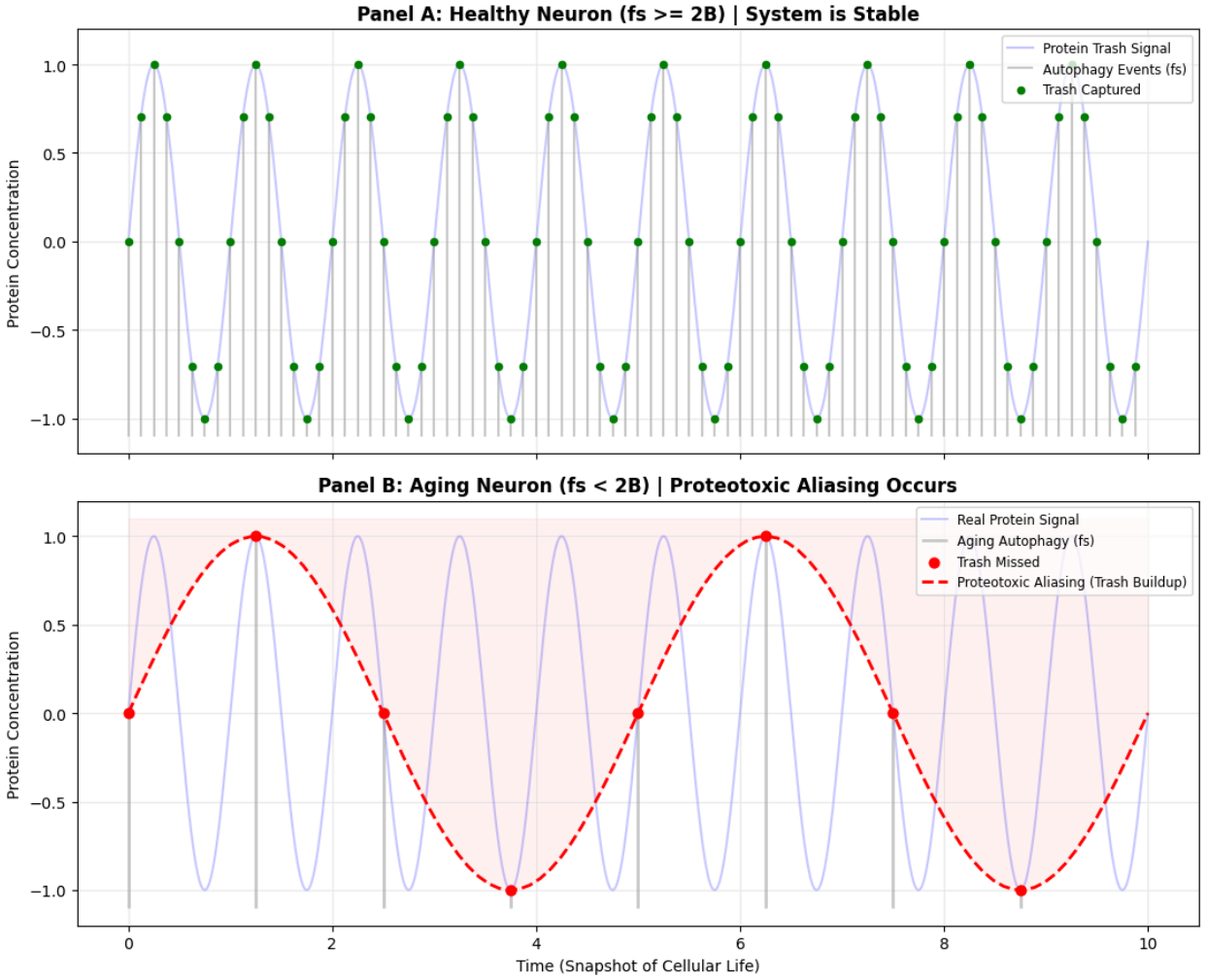
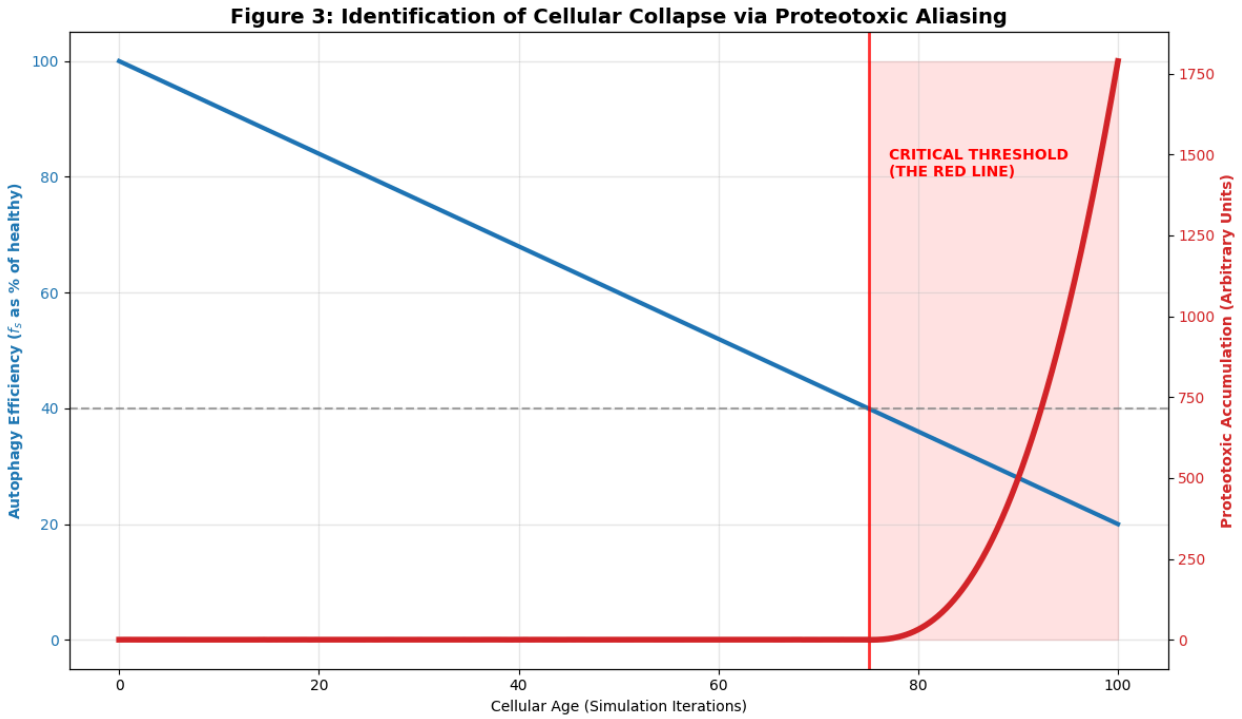


Figure 3: Identification of Cellular Collapse via Proteotoxic Aliasing



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