Denoise Stepwise Signals by Diffusion Model

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Stepwise signals are ubiquitous in single-molecule detections, representing critical molecular conformational changes or state transitions. However, these features are often obscured by background noise. The traditional frequency-domain filtering or Hidden Markov Model (HMM)–based approaches face significant limitations in edge preservation and stationarity assumptions [1,2]. Here, we propose the Stepwise Signal Diffusion Model (SSDM), a generative framework based on the denoising diffusion probabilistic model [3]. During training, SSDM learns the statistical structure of stepwise signals via a forward diffusion process that progressively adds noise. Afterwards, it reconstructs noise-free signals from noisy input in the reverse process, incorporating a multi-scale convolutional network and an attention mechanism [4], as shown in Figure 1 (a). Comparisons on simulated datasets demonstrate that SSDM consistently outperforms traditional methods in both signal level reconstruction and transition time point detection, illustrated in Figure 1 (b). Notably, SSDM maintains strong overall performance even under severe noise conditions with SNR < 1. The robustness of SSDM is further validated on experimental data from sm-FRET [5] and nanopore DNA translocation [6]. The typical examples are shown in Figure 1 (c). Overall, SSDM offers a general and efficient framework for biophysical signal denoising, facilitating further data analysis.

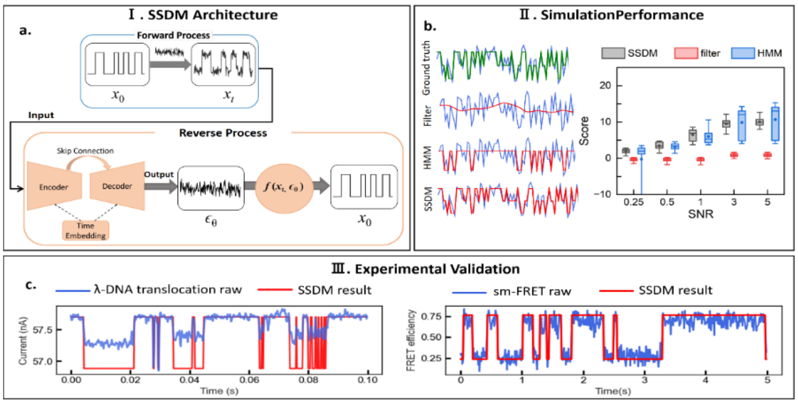

Figure 1: SSDM framework and its validation. (a) Architecture of the SSDM. (b) Signal denoising examples from different methods (left); quantitative comparison with traditional filter and HMM methods (right). (c) Application to experimental nanopore λ-DNA translocation (left) and sm-FRET trajectories (right).

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