

Kristofor Nyquist

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Experience

Pacific Biosciences

Menlo Park, CA

Senior Manager, Biophysics and Analysis

2019–present

Scientist in Reagent's R&D with proven track record evidenced by increasing levels of responsibility. Currently lead a team of 7 PhD scientists with backgrounds in single-molecule microscopy, molecular modeling, physical modeling, and statistics. We work on understanding fundamental issues that limit the throughput of Pacbio's single-molecule long-read DNA sequencing technology.

Highlights:

- Oversaw projects that have shaped how we understand the causes of read terminations so that we know where research should focus.
- Led statistical modeling efforts to scope out the expected performance of different next-generation long-read sequencer designs, ultimately contributing to the selection of our next-gen target platform.
- Characterized the kinetic signature of 5mC methylation, establishing the feasibility of 5mC detection without extra sample prep or sequencing. 5mC calling was the main feature of our last system release (Sequel IIe v11).
- Experimentally discovered a design principle for improving Pacbio's polymerase replication activity near a surface. Continues to be used in our released chemistry.

Pendulum Therapeutics

San Francisco, CA

Senior Software Engineer

2018–2019

Software engineer focused on building scalable cloud infrastructure for automating large-scale bioinformatics analyses such as metagenome assembly, isolate assembly, and 16S rRNA metagenome profiling.

Highlights:

- Designed and built cloud-based cluster computing system for executing massively scalable data analysis projects. System was designed to support workflow graphs of arbitrary size/shape/complexity, to be failure tolerant, and to be cost effective.
- Designed and built a RESTful system for storing, versioning, and querying genomes as well as genome annotations.
- Wrote high-throughput liquid-handling workflows for performing 16S-sequencing sample prep (96-well) as well as qPCR sample prep (384-well). Integrated protocols and liquid handlers with the company's custom-written LIMS system.

Pacific Biosciences

Menlo Park, CA

Senior Scientist

2015–2018

Scientist in biochemistry group. Focused on developing software tools that help guide experimental assays for finding DNA polymerase mutants with better single-molecule sequencing performance.

Highlights:

- Built automated workflows for processing and analyzing the sequencing performance of DNA polymerase mutants. Identified polymerase mutants with 2x the sequencing readlength and 3% better raw accuracy.
- Developed algorithms for identifying false-positive basecalls. Demonstrated gains in raw-accuracy of 2% and worked with software teams to integrate algorithms into production.
- Developed methods to experimentally measure polymerase processivity. Contributed to the discovery that certain sequencing applications could have 3x the throughput with simple modifications to sample-preparation.
- Discovered sample-prep conditions that increased background noise and worked with biochemistry team to eliminate the problem.

University of California, Berkeley

Berkeley, CA

PhD Student

2010–2015

Graduate student researcher in Andreas Martin's lab, co-supervised by Carlos Bustamante.

Highlights:

- Doctoral thesis focused on the mechanical characterization of a bacterial proteolytic motor, ClpXP. We directly measured its velocity, maximal force generation, and basic step size using an optical trap.
- Developed suite of tools to analyze optical tweezers data, including maximum-likelihood algorithms to automatically detect and fit underlying steps in non-stationary, noisy time-series data.
- Cloned/expressed/purified large protein complexes and developed assays to monitor their activity.
- Built three-color objective-TIRF microscope for conducting single-molecule FRET and co-localization experiments.

Washington State University

Undergraduate Researcher

Undergraduate researcher in Doerte Blume's lab doing analytical and computational modeling of ultracold many-atom systems.

Pullman, WA

2008–2010

Highlights:

- Developed algorithms to simulate the self-organization of ultracold many-atom systems.
- Implemented molecular dynamics simulations and simulated-annealing probabilistic models.

Relevant Skills

Languages: Python, Bash, MATLAB, Javascript, SQL, C/C++

Tools: snakemake, numpy, pandas, scikit-learn, jupyter, AWS, docker, luigi, git, flask, django, plotly

Lab: molecular biology, enzyme kinetics, spectroscopy, fluorescence microscopy, single-molecule biophysics, lab automation

Education

University of California, Berkeley

PhD, Biophysics

Berkeley, CA

2010–2015

Washington State University

BS, Physics

Pullman, WA

2006–2010

Publications

Fukuda H, Yamaguchi D, Nyquist K, et al. Father-to-offspring transmission of extremely long *NOTCH2NLC* repeat expansions with contractions: genetic and epigenetic profiling with long-read sequencing. *Clin Epigenet.* 2021;13(204)

Nyquist K and Martin A. Marching to the beat of the ring: polypeptide translocation by AAA+ proteases. *Trends Biochem Sci.* 2014;39(2):53-60

Sen M*, Maillard R*, Nyquist K* et al. The ClpXP protease unfolds substrates using a constant rate of pulling but different gears. *Cell.* 2013;155(3):636-646

PhD Dissertation:

Nyquist K. Mechanism of Protein Unfolding and Polypeptide Translocation by the AAA+ Protease ClpXP. UC Berkeley. 2015. Accession permalink <https://escholarship.org/uc/item/5kr7t56k>

Patents

Miller E, Bjornson K, Nyquist K, Kamtekar S. Methods and Compositions for Enriching Compositions for Polymerase Enzyme Complexes. US Patent Application 20170356041. Filed June 9, 2017

Awards

National Science Foundation Graduate Research Fellowship

2012–2015

National Institutes of Health Molecular Biophysics Training Grant

2010–2012

NASA Space Grant

2009