

# Nanopore automata

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## 1 Abstract

State machine algorithms for aligning Nanopore reads.

## 2 Specification

Initial goal (Preliminary Results) is simple reusable code for aligning a segmented nanopore read (with segment currents summarized) to a reference sequence.

Longer-term goals (Specific Aims) include

- quasi-hierarchical series of models for processed→raw data (raw, FAST5, FASTQ, FASTA)
- transducer intersection-style models for read-pair alignment
- systematic strategies for approximation/optimization algorithms, climbing the hierarchy (starting with k-mer or FM-index approaches)
- transducer intersection models for aligning reads from different sequencing technologies

### 2.1 Parameterization algorithm

Given the following inputs

- Reference genome (FASTA)
- Segment-called reads (FAST5/HDF5)

Perform the following steps

- Perform Baum-Welch to fit a rich model

Rich model incorporates segment statistics.

## 2.2 Reference search algorithm

Given the following inputs

- Reference genome
- Segment-called reads (FAST5/HDF5)
- Parameterized rich model

Perform the following steps

- Perform Viterbi alignment

## 2.3 Implementation

Libraries etc.

HDF5...

## 2.4 Evaluation

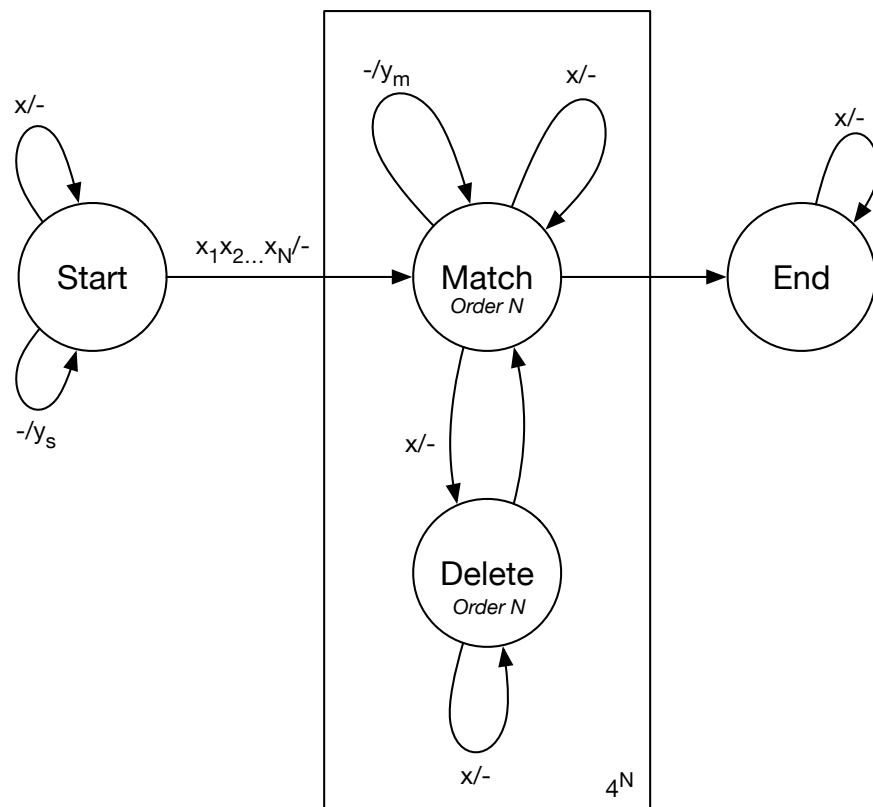
Strategy...

Data sets...

# 3 Methods

Model & inference algorithms.

### 3.1 Model



- Order- $N$  transducer.
- Input: nucleotide alphabet  $\Omega$
- Output: real numbers signifying current levels  $\Re$
- States: **Start**,  $\text{Match}_{x_1 \dots x_N}$ ,  $\text{Delete}_{x_1 \dots x_N}$ , **End**

Transitions:

Source	Destination	Weight	Absorbs	Emits
Start	Start	$p^{\text{StartEmit}}$		$y_s \sim \text{Normal}(\mu^{\text{Start}}, \tau^{\text{Start}})$
Start	Start	1	$x \in \Omega$	
Start	$\text{Match}_{x_1 \dots x_N}$	$1 - p^{\text{StartEmit}}$	$x_1 \dots x_N \in \Omega^N$	
$\text{Match}_{x_1 \dots x_N}$	$\text{Match}_{x_1 \dots x_N}$	$p^{\text{MatchEmit}}_{x_1 \dots x_N}$		$y_m \sim \text{Normal}(\mu^{\text{Match}}_{x_1 \dots x_N}, \tau^{\text{Match}}_{x_1 \dots x_N})$
$\text{Match}_{x_1 \dots x_N}$	$\text{Match}_{x_2 \dots x_{N+1}}$	$(1 - p^{\text{MatchEmit}}_{x_1 \dots x_N})$ $\times (1 - p^{\text{BeginDelete}})$	$x_{N+1} \in \Omega$	
$\text{Match}_{x_1 \dots x_N}$	$\text{Delete}_{x_2 \dots x_{N+1}}$	$(1 - p^{\text{MatchEmit}}_{x_1 \dots x_N})$ $\times p^{\text{BeginDelete}}$	$x_{N+1} \in \Omega$	
$\text{Match}_{x_1 \dots x_N}$	End	$1 - p^{\text{MatchEmit}}_{x_1 \dots x_N}$		
$\text{Delete}_{x_1 \dots x_N}$	$\text{Delete}_{x_2 \dots x_{N+1}}$	$p^{\text{ExtendDelete}}$	$x_{N+1} \in \Omega$	
$\text{Delete}_{x_1 \dots x_N}$	$\text{Match}_{x_1 \dots x_N}$	$1 - p^{\text{ExtendDelete}}$		
End	End	1	$x \in \Omega$	

### 3.2 Baum-Welch algorithm

As usual.

### 3.3 Viterbi algorithm

As usual.

## 4 Results

## 5 Discussion

## **6 Acknowledgments**

## **7 Figure Legends**



## 8 Appendix

### 8.1 Exponential distribution

$$\begin{aligned}
 x &\sim \text{Exponential}(\kappa) \\
 P(x|\kappa) &= \kappa \exp(-\kappa x) \\
 \mathbb{E}[x] &= \kappa^{-1} \\
 \text{Var}[x] &= \kappa^{-2}
 \end{aligned}$$

Rate parameter  $\kappa$ .

### 8.2 Gamma distribution

$$\begin{aligned}
 x &\sim \text{Gamma}(\alpha, \beta) \\
 P(x|\alpha, \beta) &= \frac{x^{\alpha-1} \beta^\alpha \exp(-x\beta)}{\Gamma(\alpha)} \\
 \mathbb{E}[x] &= \alpha/\beta \\
 \text{Var}[x] &= \alpha/\beta^2
 \end{aligned}$$

Shape parameter  $\alpha$ , rate parameter  $\beta$ .  $\Gamma()$  is the gamma function

$$\Gamma(\alpha) = \int_0^\infty z^{\alpha-1} \exp(-z) dz$$

Note  $\Gamma(n) = (n-1)!$  for positive integer  $n$ .

### 8.3 Normal distribution

$$x \sim \text{Normal}(\mu, \tau)$$

Mean  $\mu$ , precision  $\tau$  (precision is reciprocal of variance).

$$P(x|\mu, \tau) = \sqrt{\frac{\tau}{2\pi}} \exp\left(-\frac{\tau}{2}(x - \mu)^2\right)$$