Detekcia tandemových opakovaní v nanopórových dátach

Eduard Batmendijn
Školiteľ: doc. Mgr. Tomáš Vinař, PhD.

18. júna 2020

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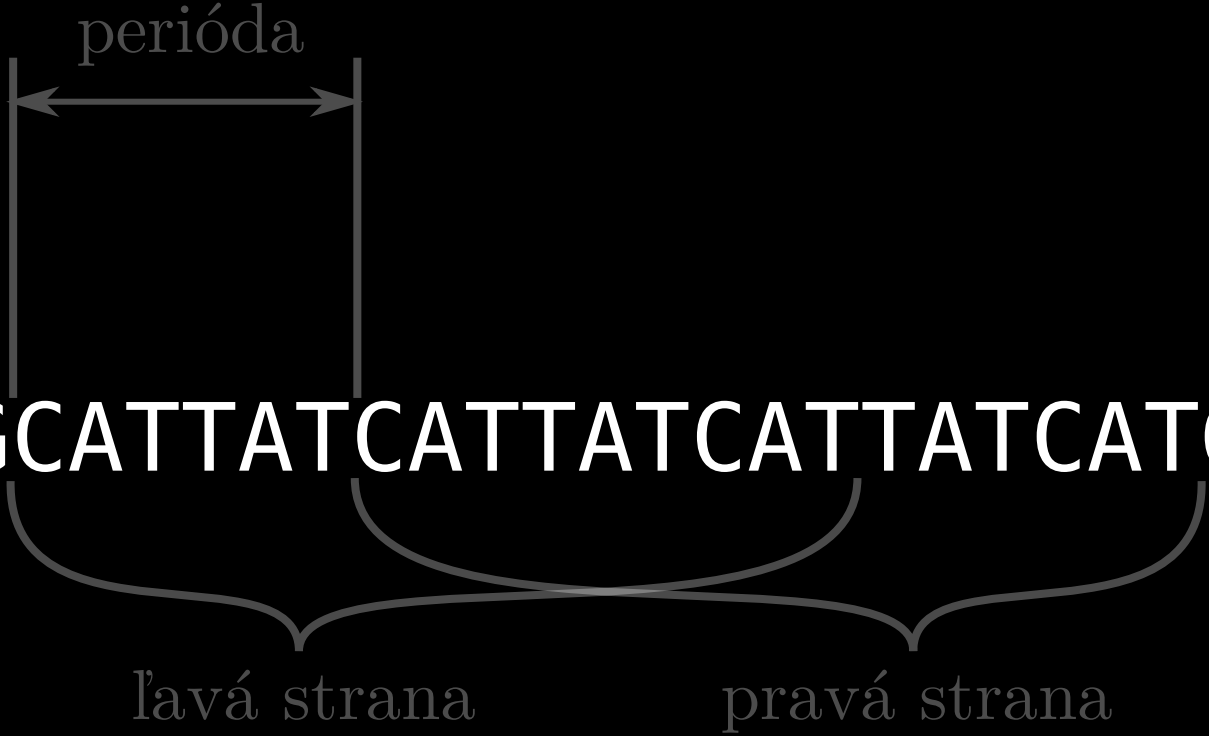
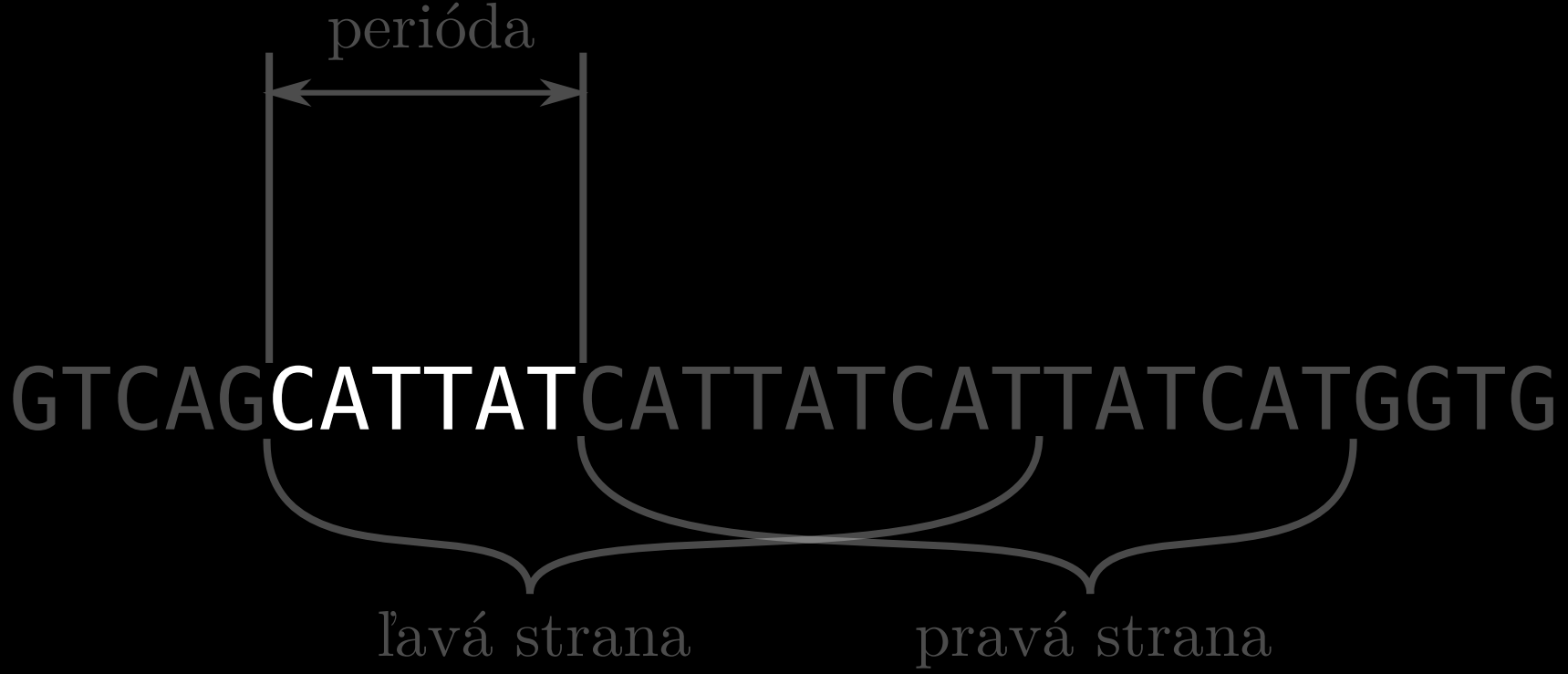
Tandemové opakovanie



Tandemové opakovanie



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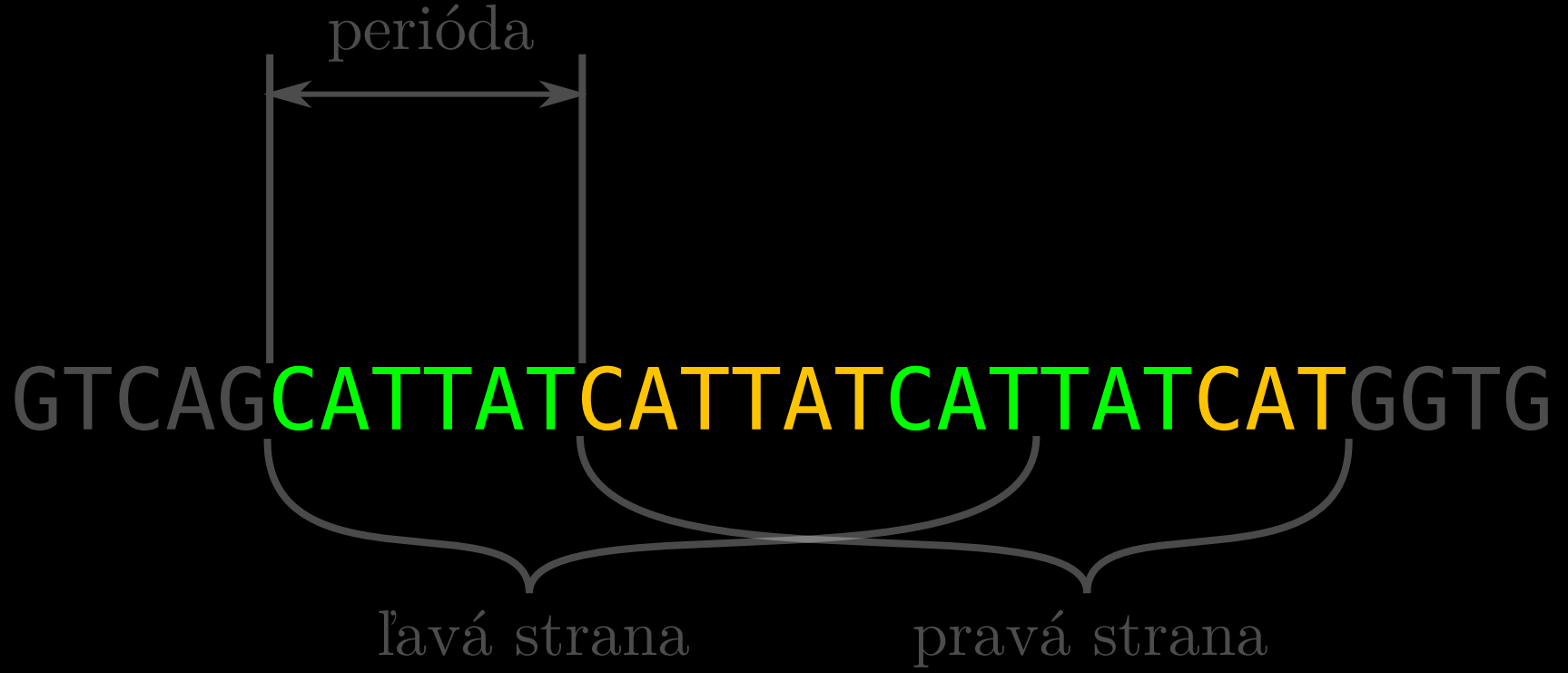

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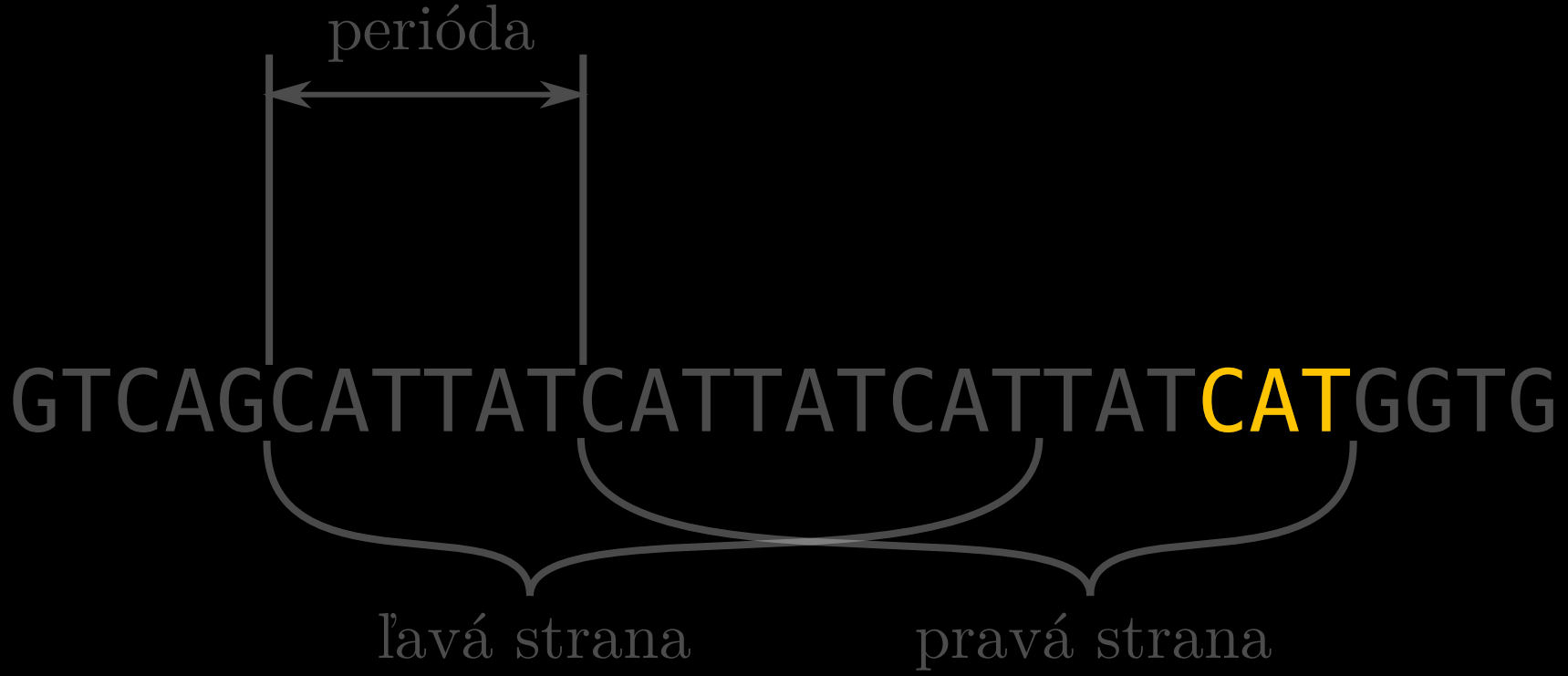

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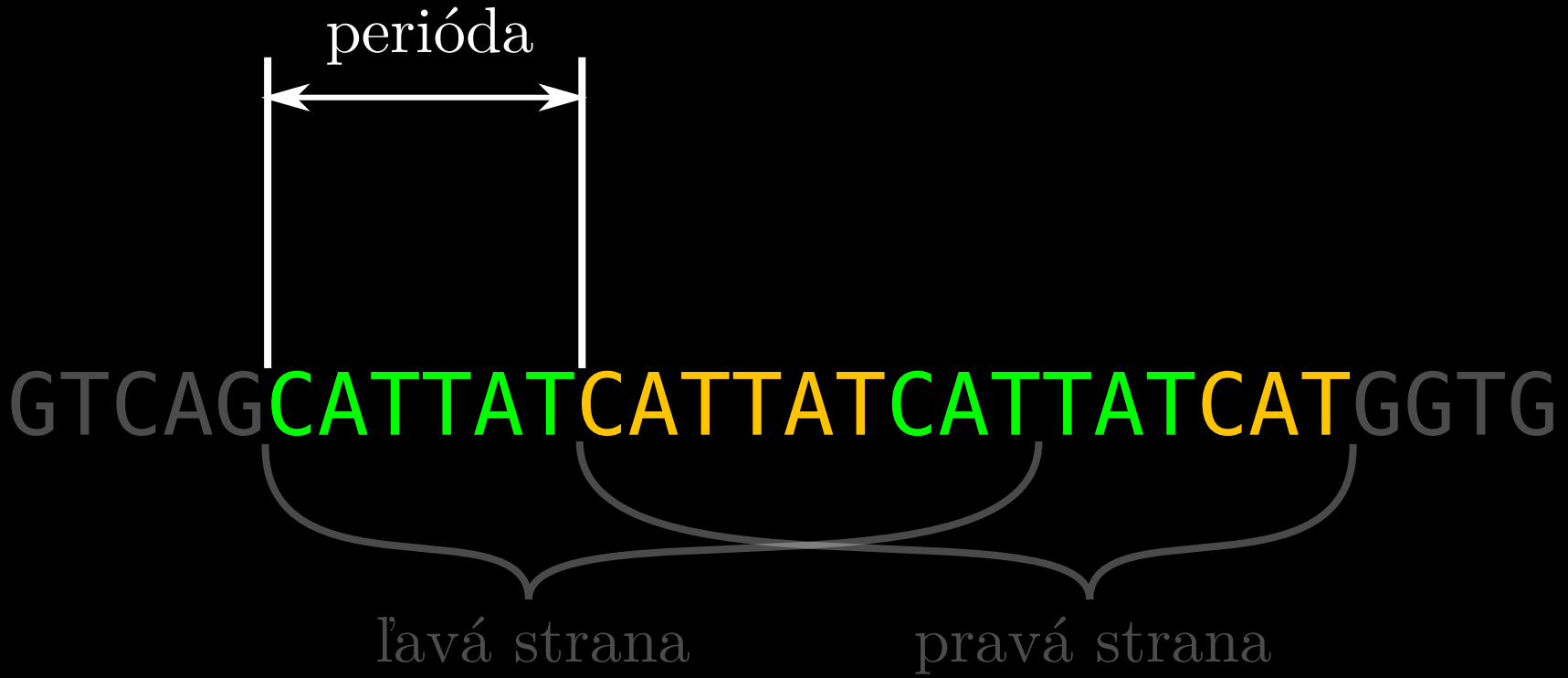

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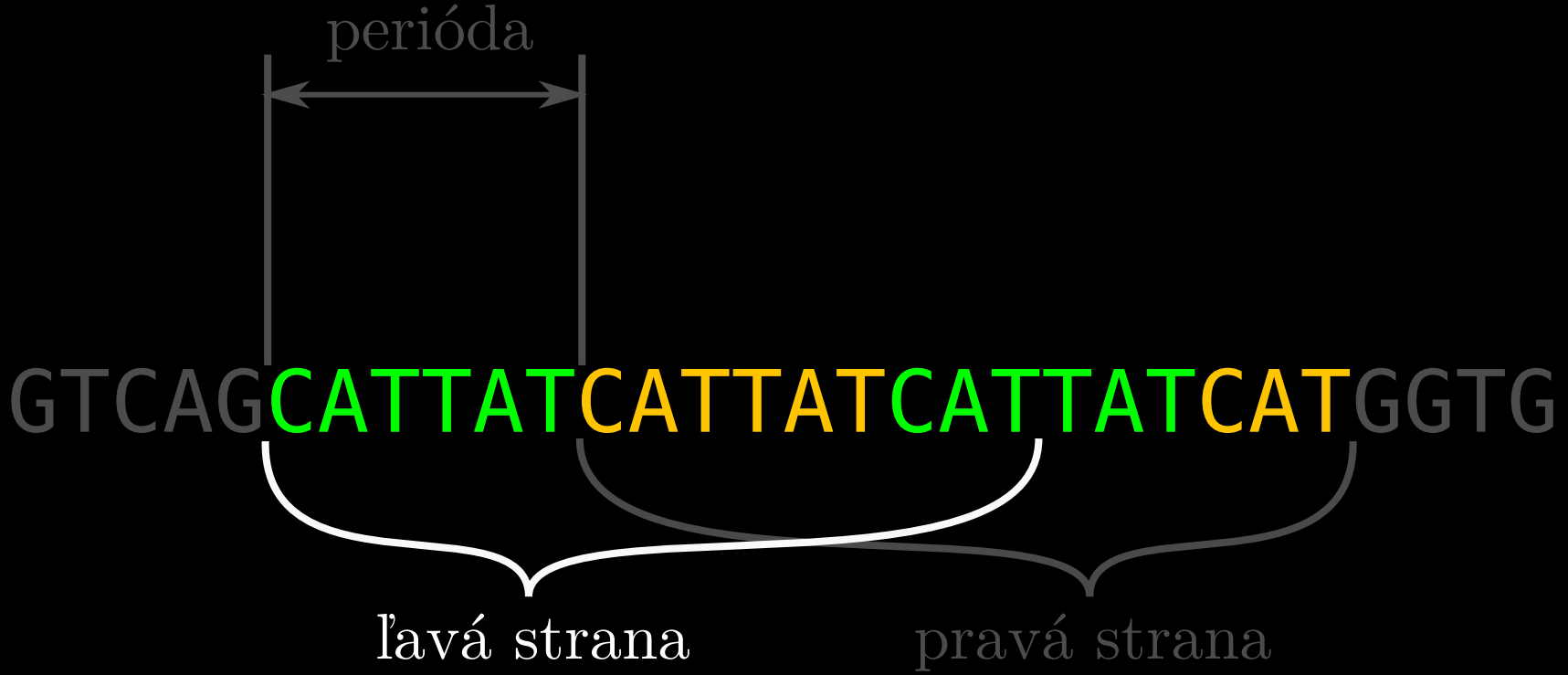

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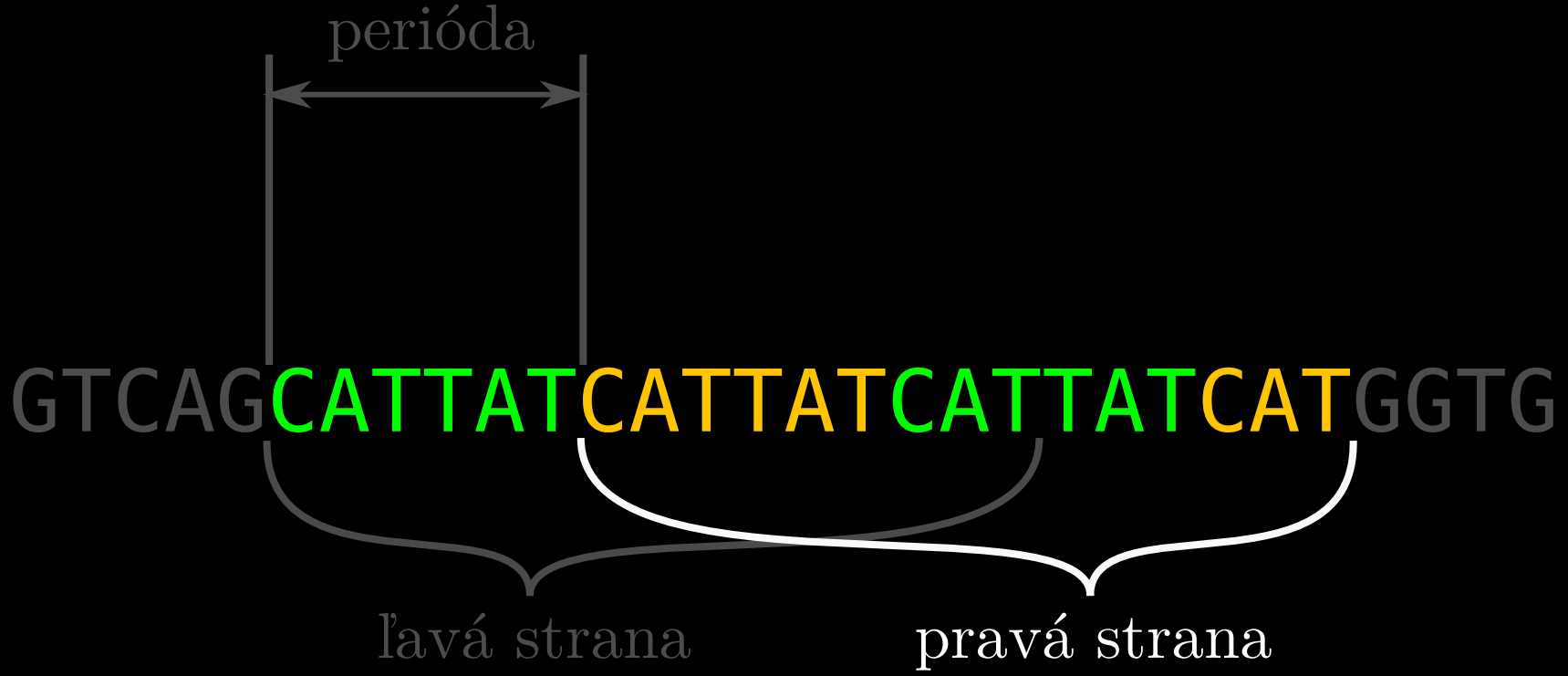

Nedokonalé tandemové opakovanie

GTCAGCATTATCATGATCATTATCATGGTG

Nedokonalé tandemové opakovanie

GTCAGCATTATCATGATCATTATCATGGTG

Detekcia tandemových opakovaní v nanopórových dátach

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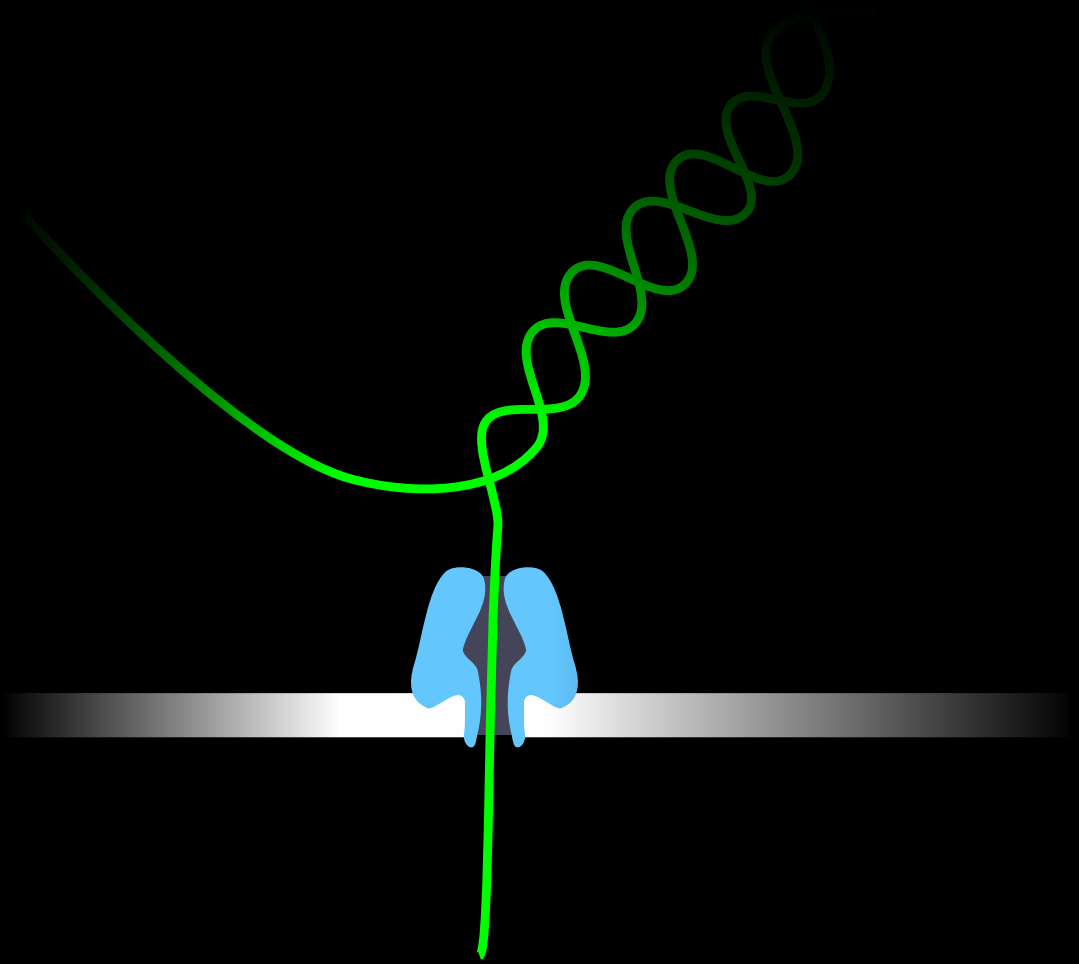
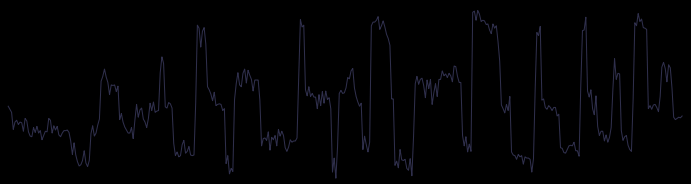
Nanopórové sekvenovanie





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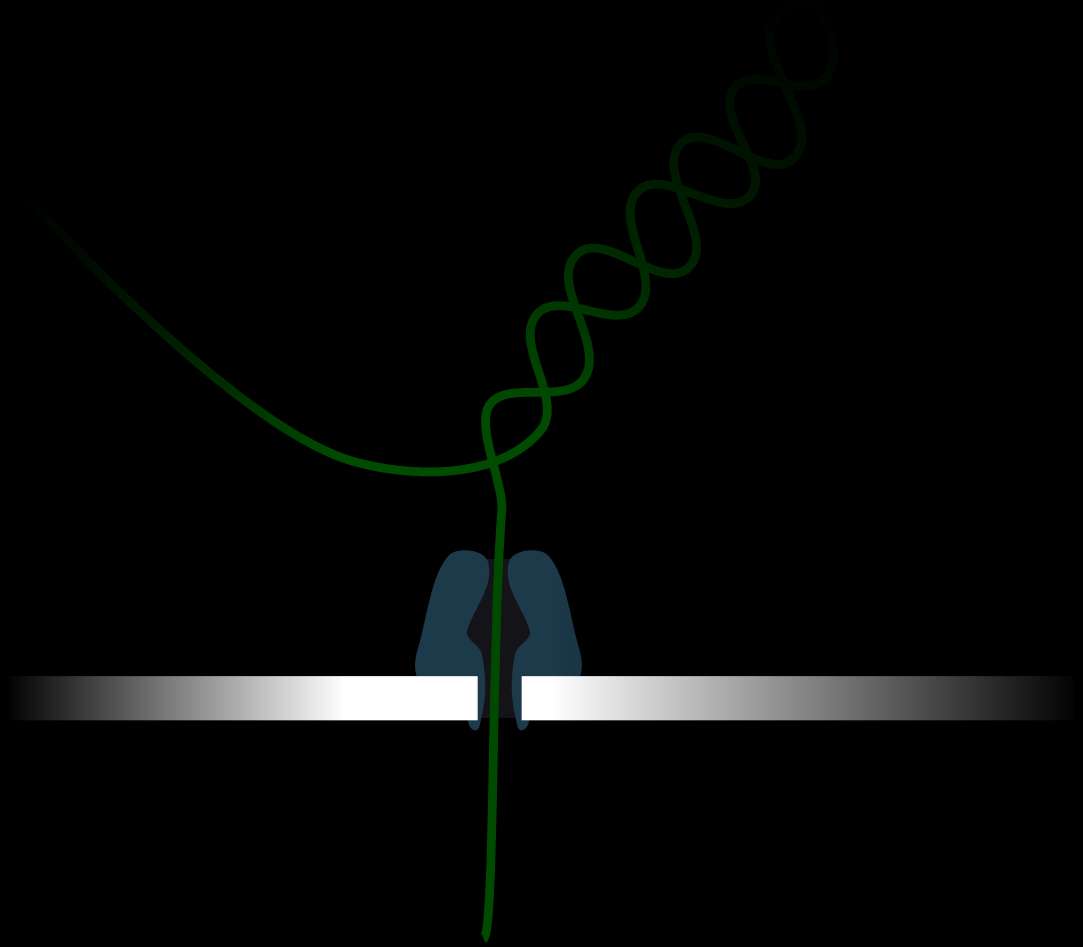
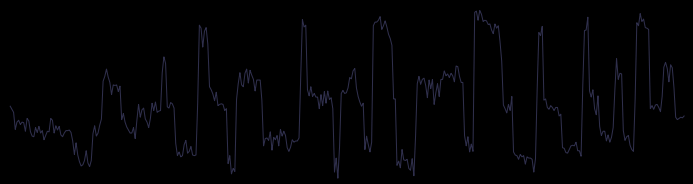
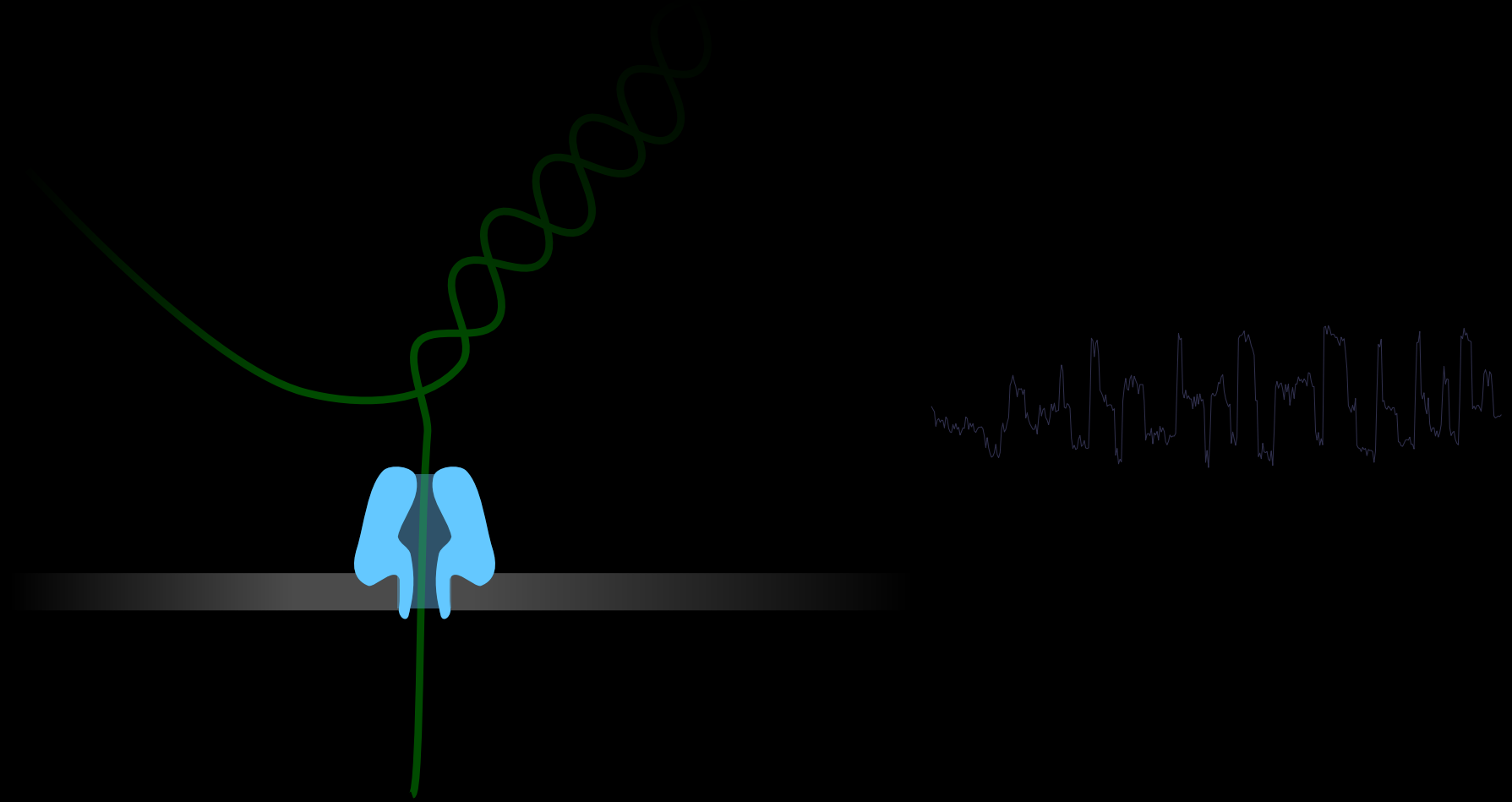




Nanopórové sekvenovanie



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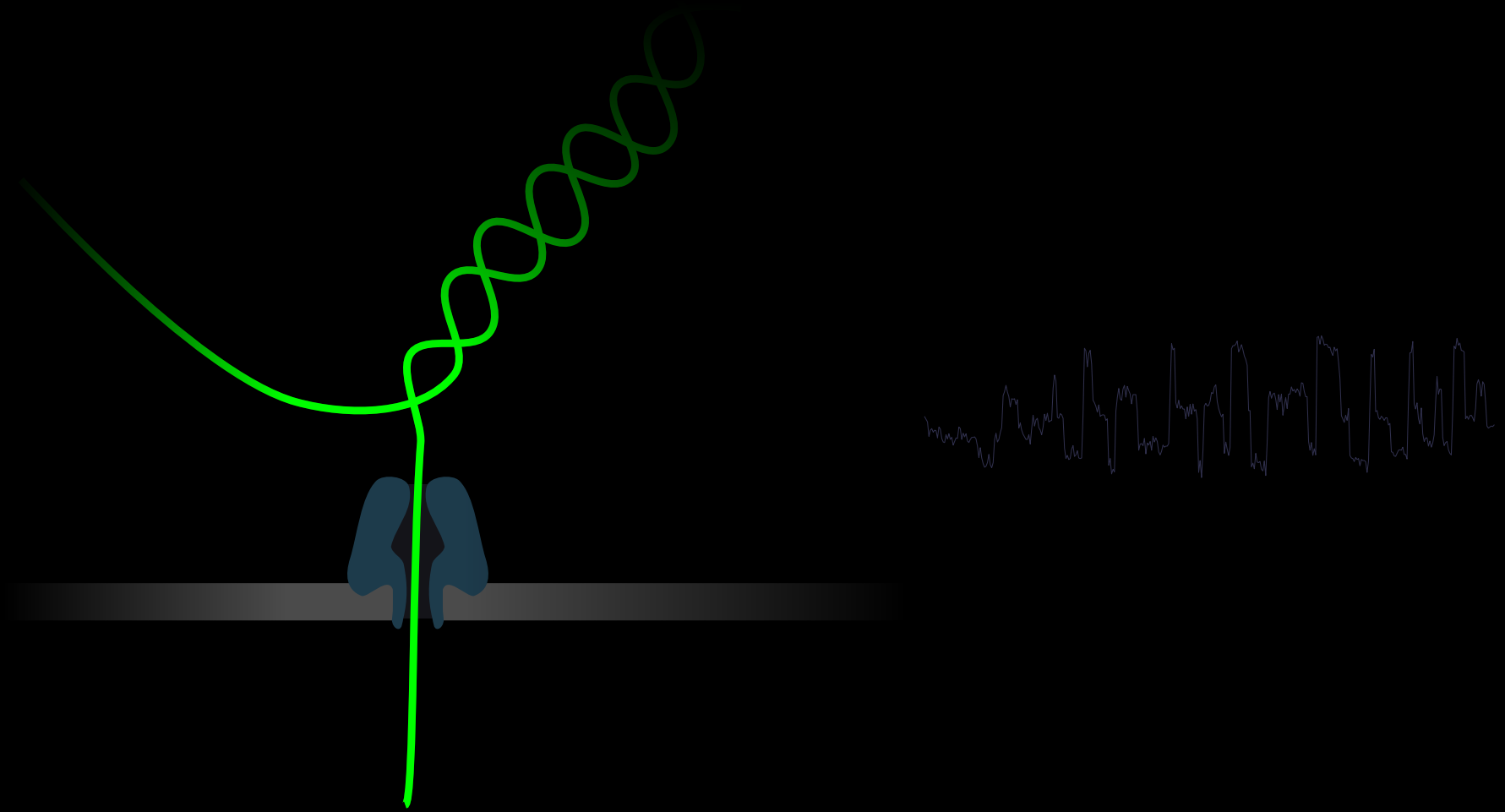

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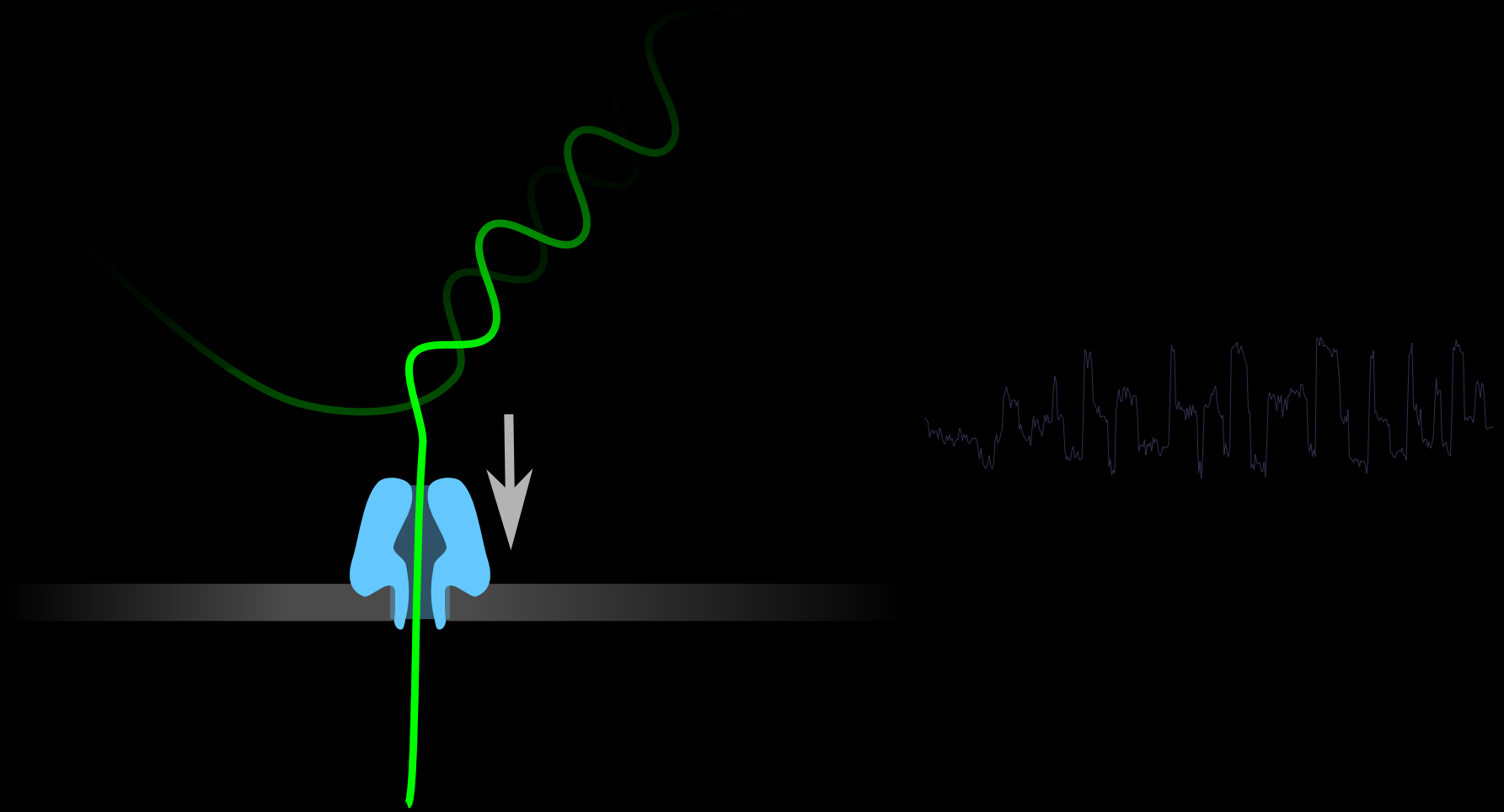

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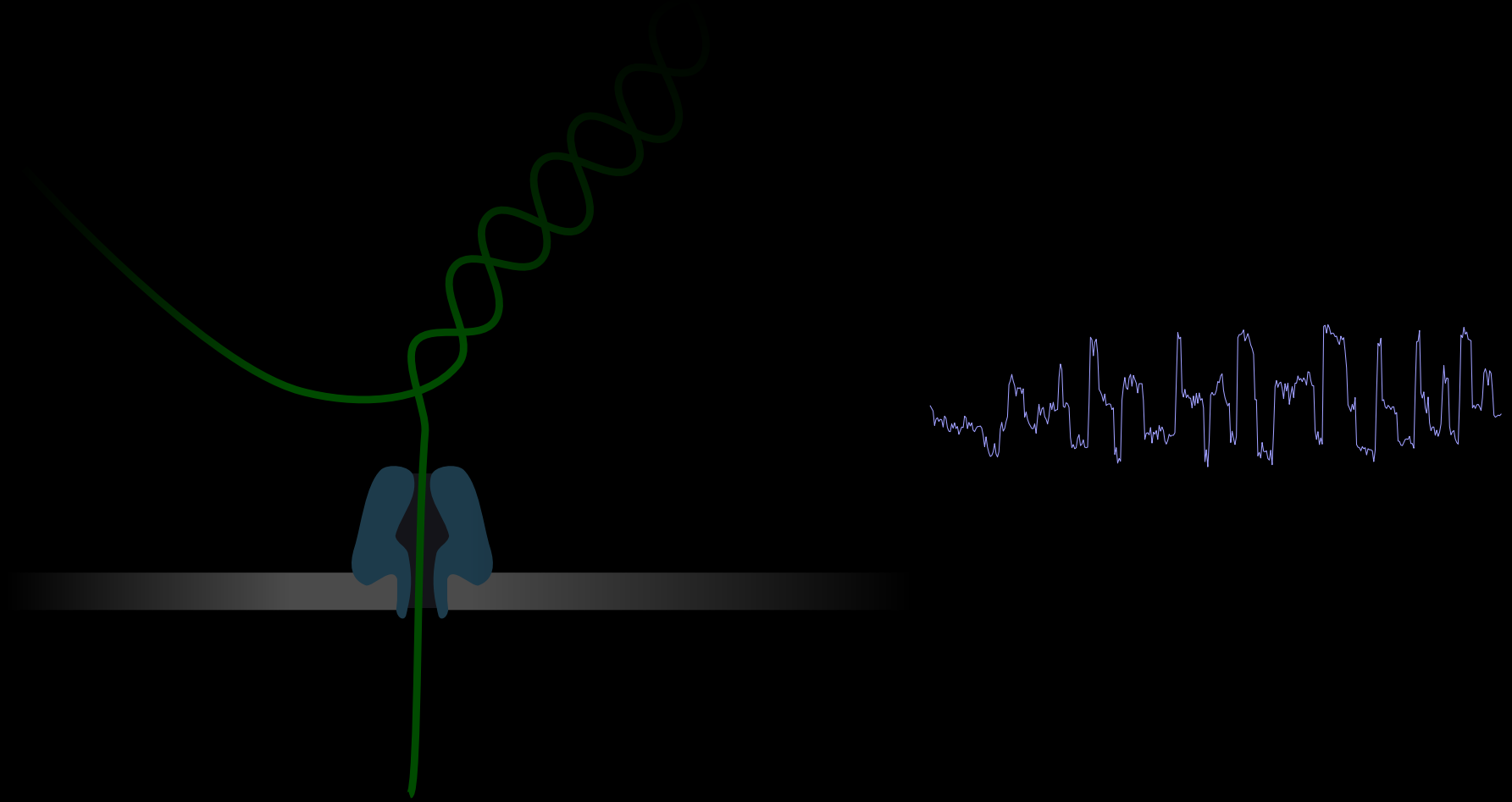
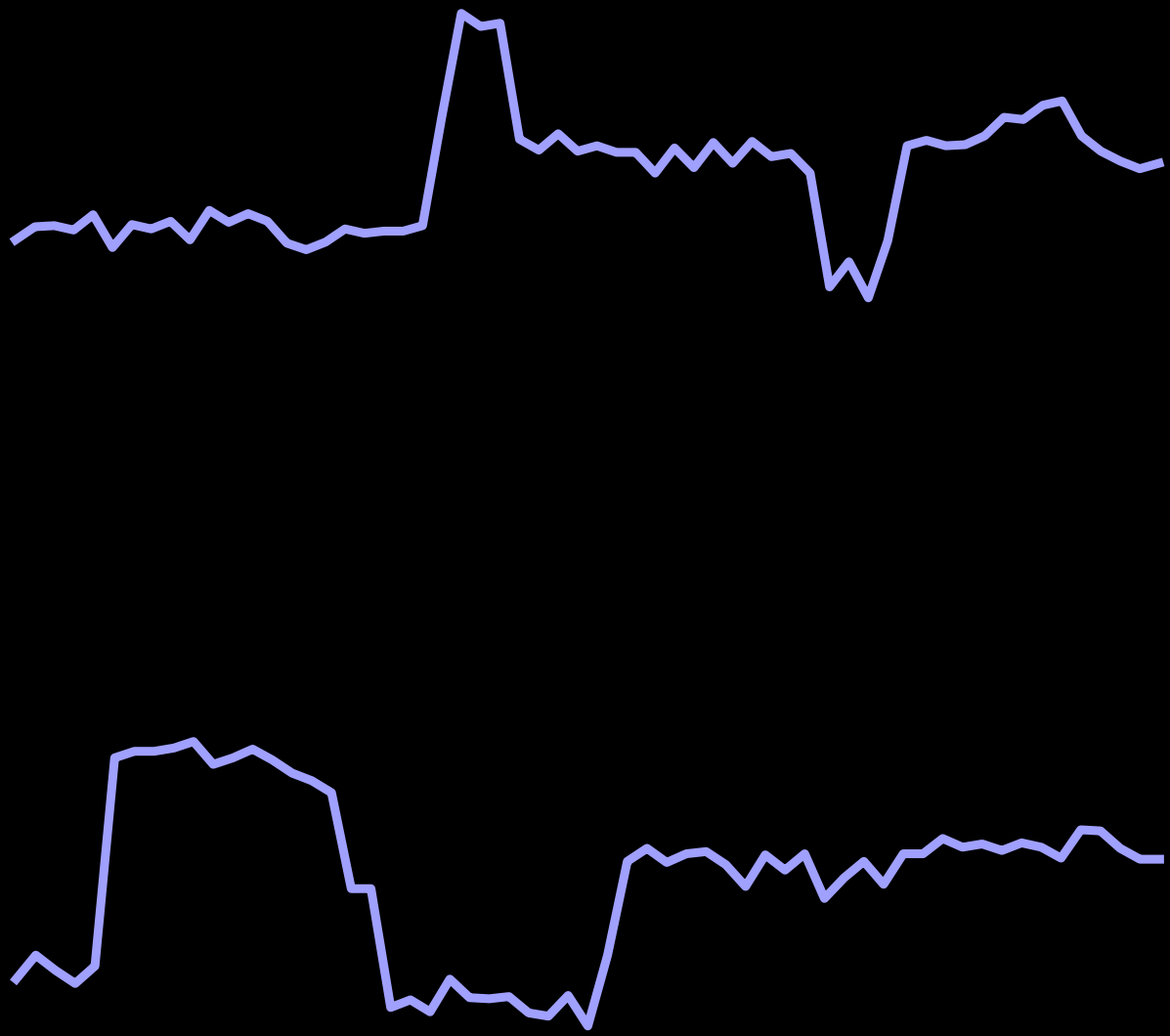


Nerovnomerná rýchlosť



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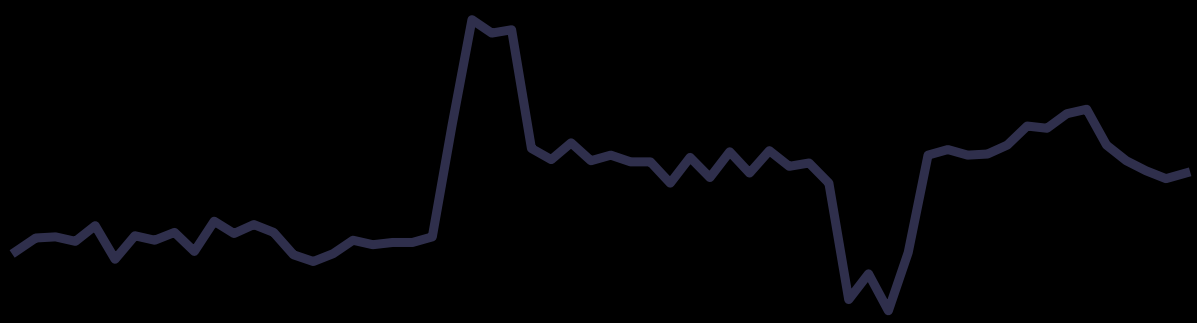
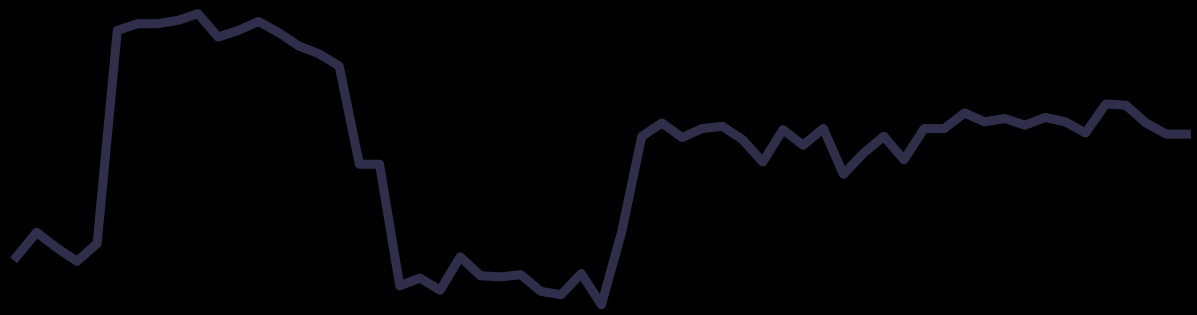


ATCATT



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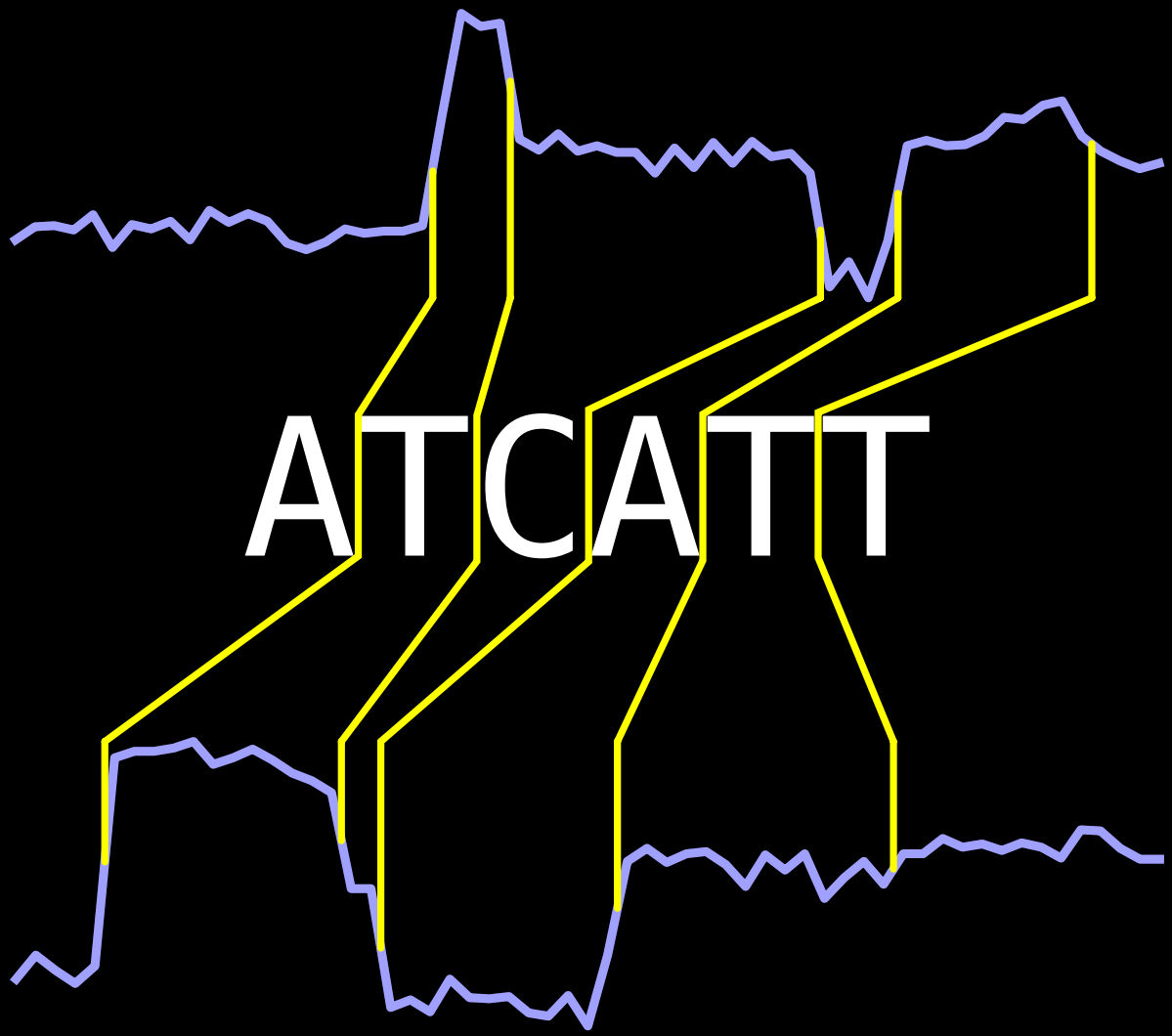
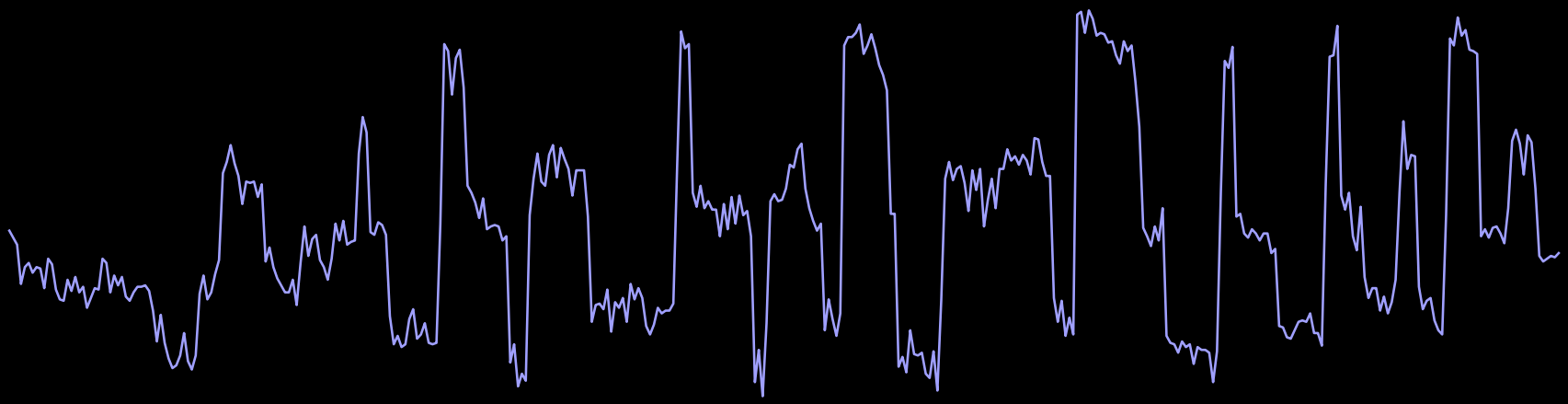
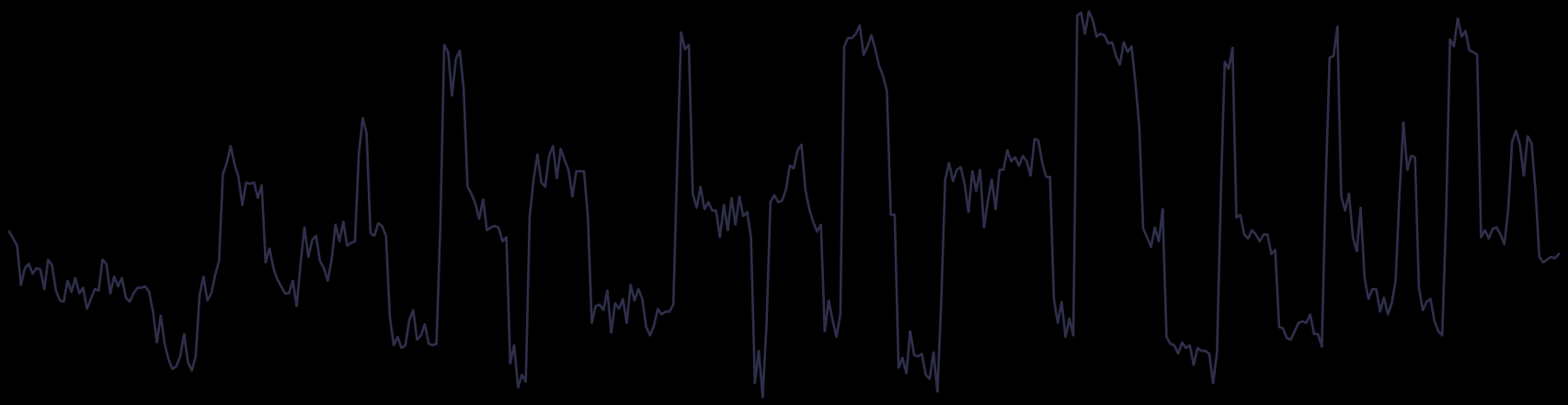


Určovanie báz (basecalling)



AAAAAAACACTTTCATCATTATCA
TTATCATTATCATCATCATATCTA

Určovanie báz (basecalling)

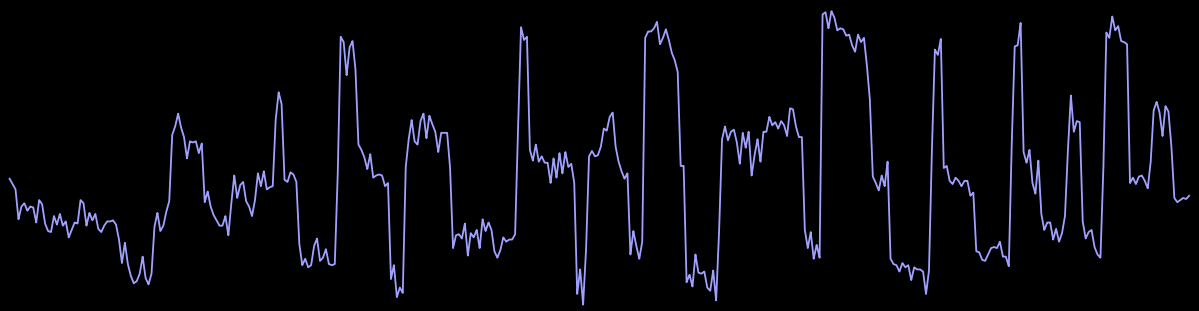


AAAAAAACACTTTCATCATTATCA
TTATCATTATCATCATCATATCTA

85% – 90%

Riešenie

Naivná detekcia



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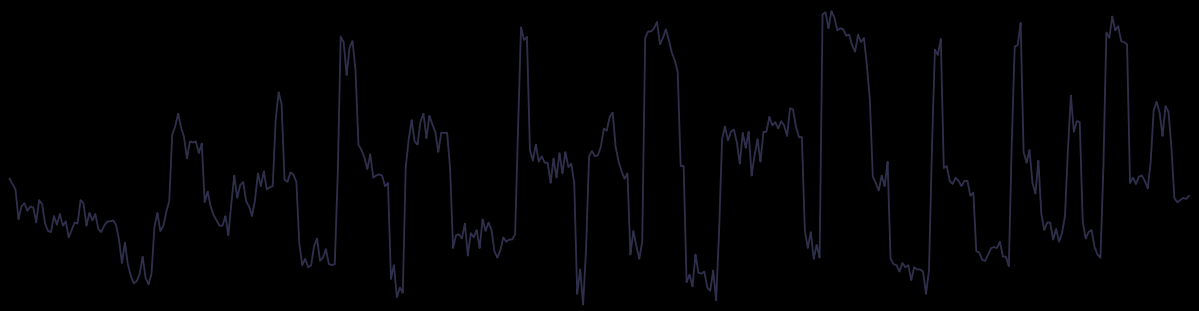
AAAAAAACACTTTCATCATTATCA
TTATCATTATCATCATCATATCTA

Naivná detekcia



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TTATCATTATCATCATCATATCTA

AAAAAAACACTTTCATCATTATCA
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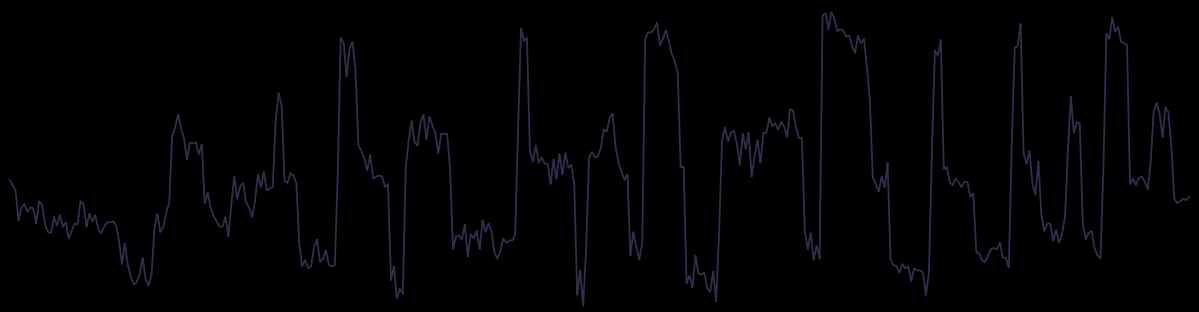

AAAAAAACACTTTCATCATTATCA
TTATCATTATCATCATCATATCTA

AAAAAAACACTTTCATCATTATCA
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Naivná detekcia

- Chybovosť prekladu
- Tvrdá predpoveď
- Nápad 1: detekcia priamo v signáli
- Nápad 2: čiastočné predspracovanie basecallerom

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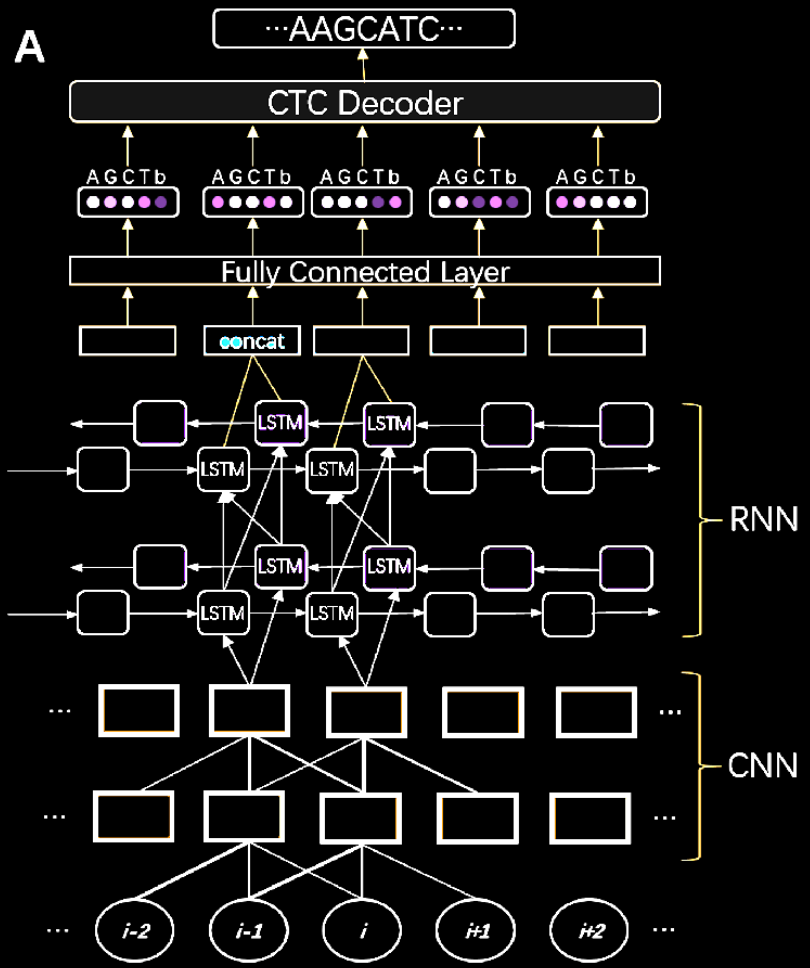
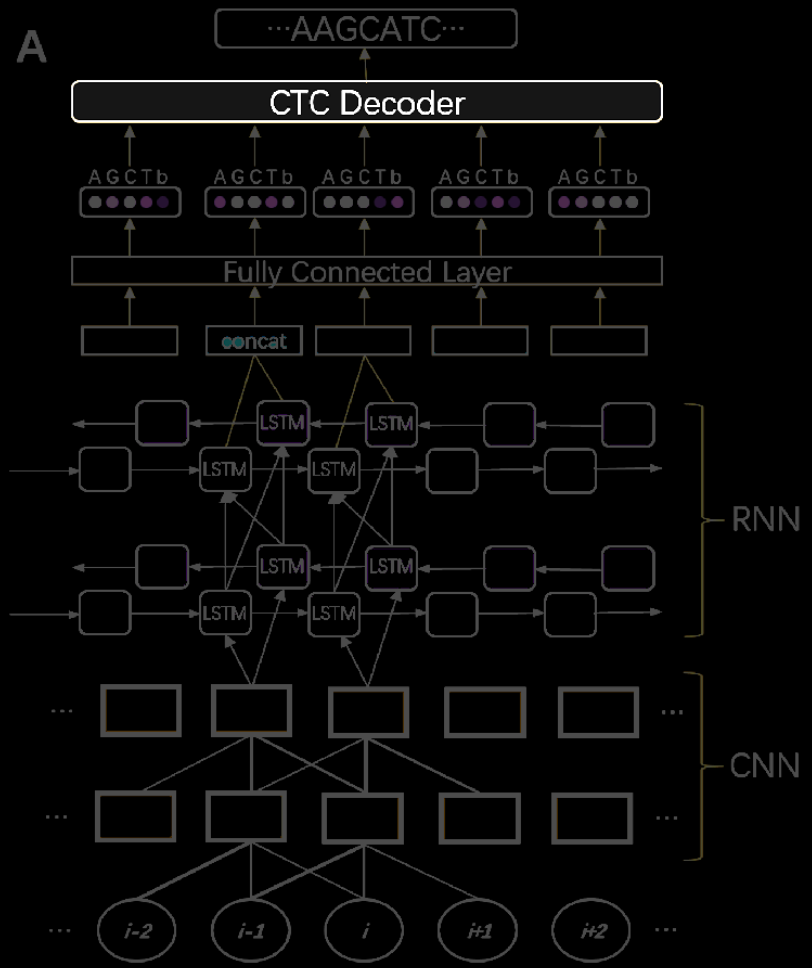
Chiron (Teng et al. 2018)



Connectionist Temporal Classification

Chiron (Teng et al. 2018)



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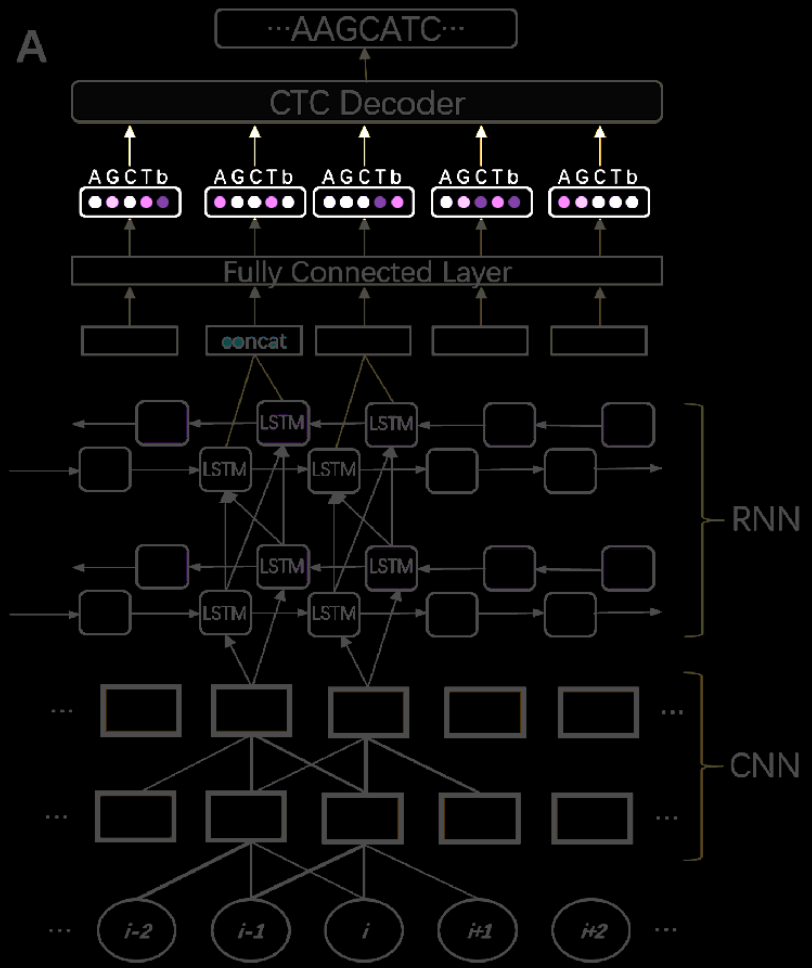
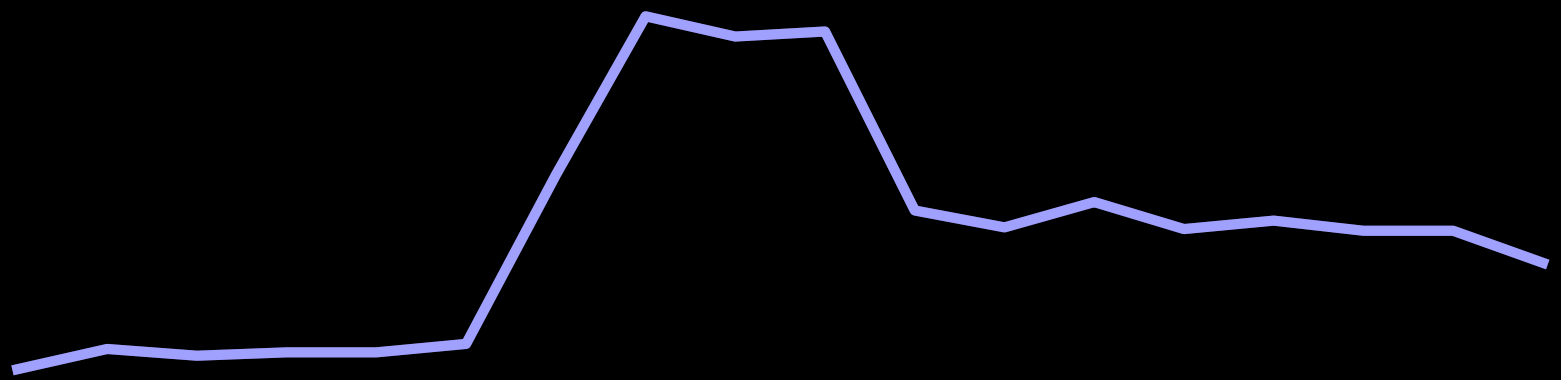


Connectionist Temporal Classification

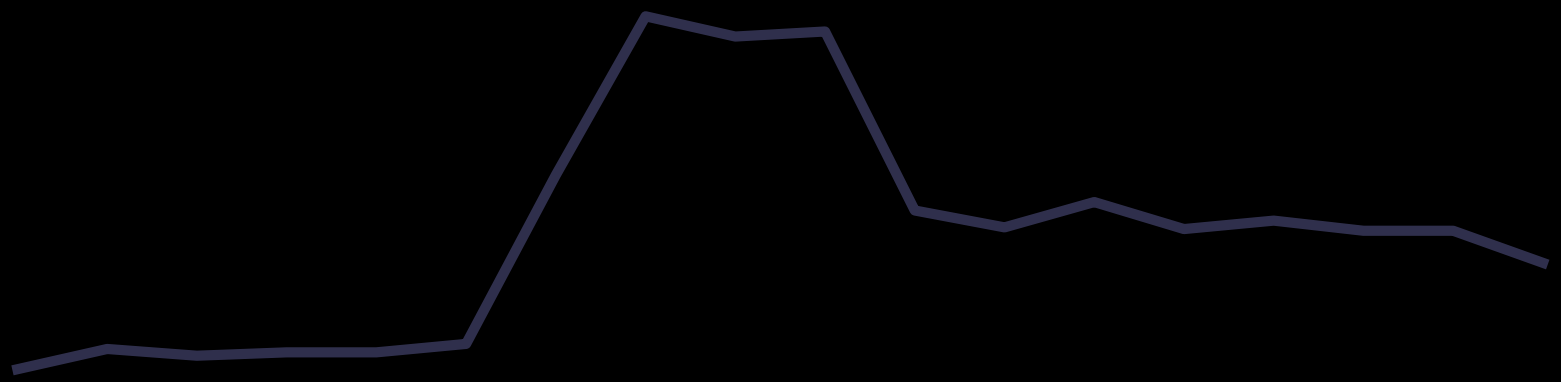
CTC anotácie



- - A A A - - T T C C - - - - - -

A T C

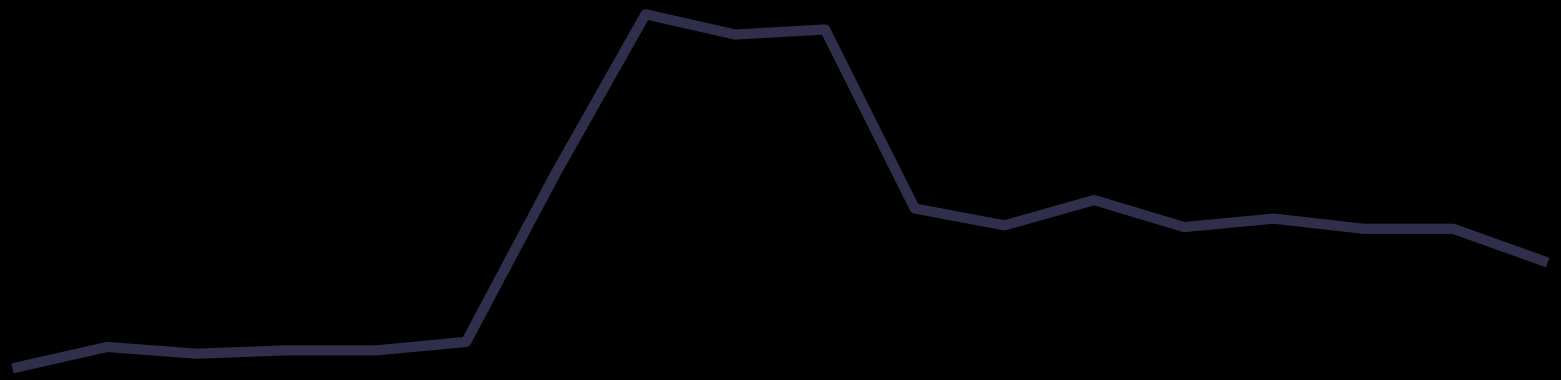
CTC anotácie



- -AAA- -TTCCC- - - - - -

A T C

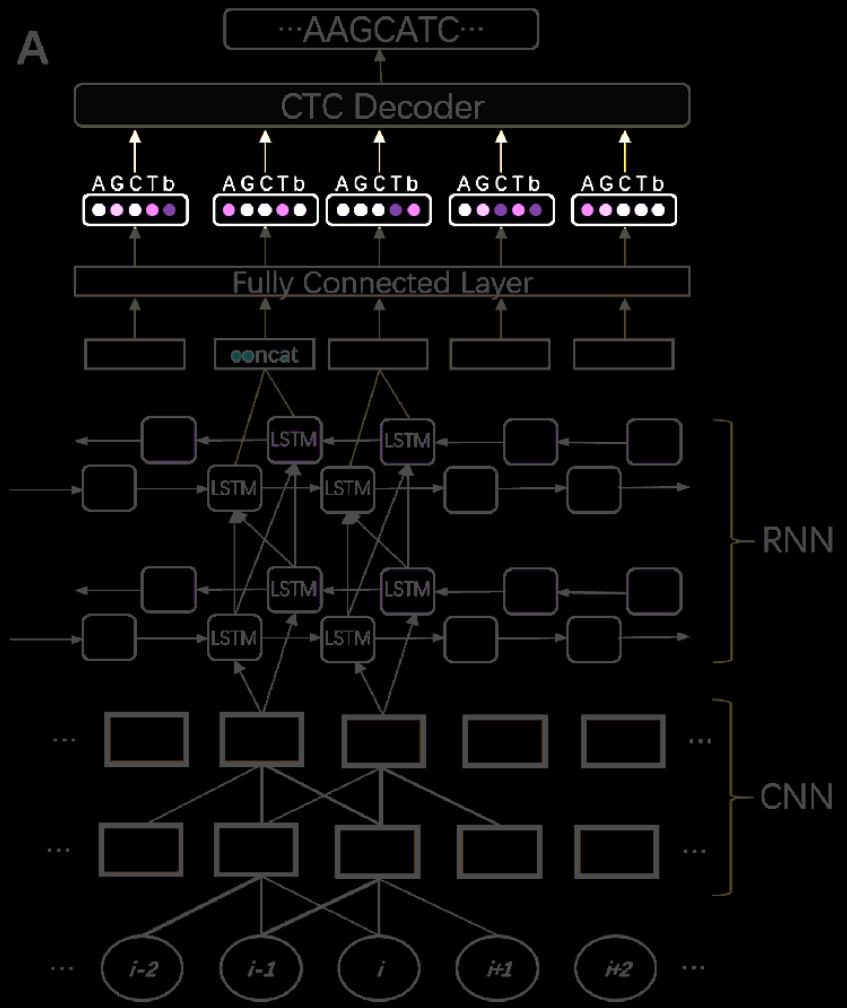
CTC anotácie



- - A A A - - T T C C - - - - - - -

A T C

CTC predpovede



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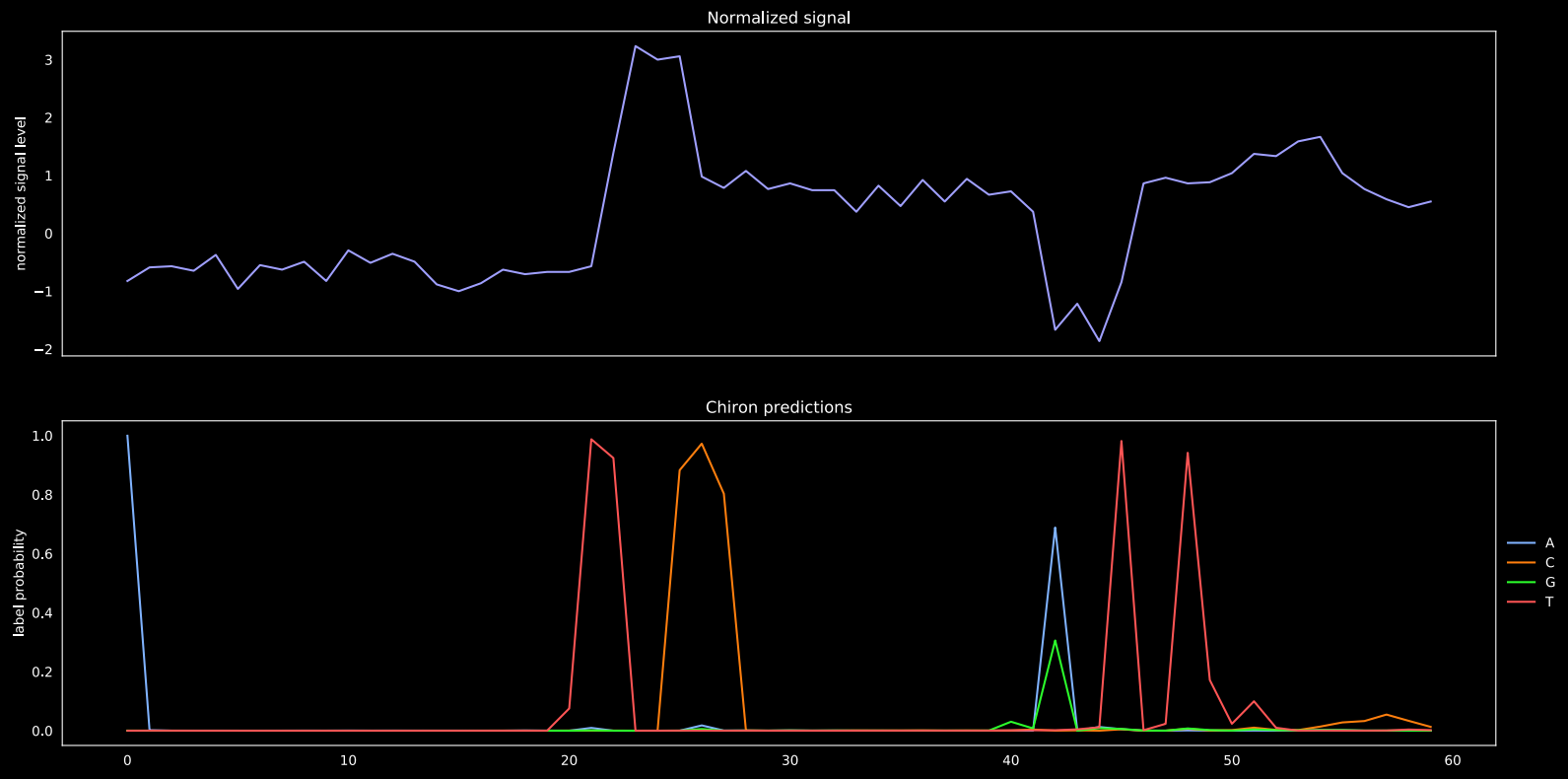

CTC dekódovanie

```
--AAA--TTCCC------
A-----T-C---------
AAAAAATTTCCCCCCCCC
ATC---------------
```

ATC

```
--AAA--GGGGG------
-A-----G----------
AAAAAAGGGGGGGGGGG
AG----------------
```

AG

CTC dekódovanie

```
--AAA--TTCCC------
A-----T-C---------
AAAAAATTTCCCCCCCCC
ATC---------------
```

ATC

```
--AAA--GGGGG------
-A-----G----------
AAAAAAGGGGGGGGGGG
AG----------------
```

AG

CTC dekódovanie

```
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A-----T-C---------
AAAAAATTTCCCCCCCCC
ATC---------------
```

ATC

```
--AAA--GGGGG------
-A-----G----------
AAAAAAGGGGGGGGGGG
AG----------------
```

AG

Detekcia v CTC predpovediach

- Tantan (Frith 2011)
- Skrytý Markovovský model (HMM)
- Rozšírenie z nukleotidov na CTC predpovede

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Rozširovanie HMM

- HMM pre nukleotidy
- blanky
- nedokonalosti
- zlučovanie rovnakých označení

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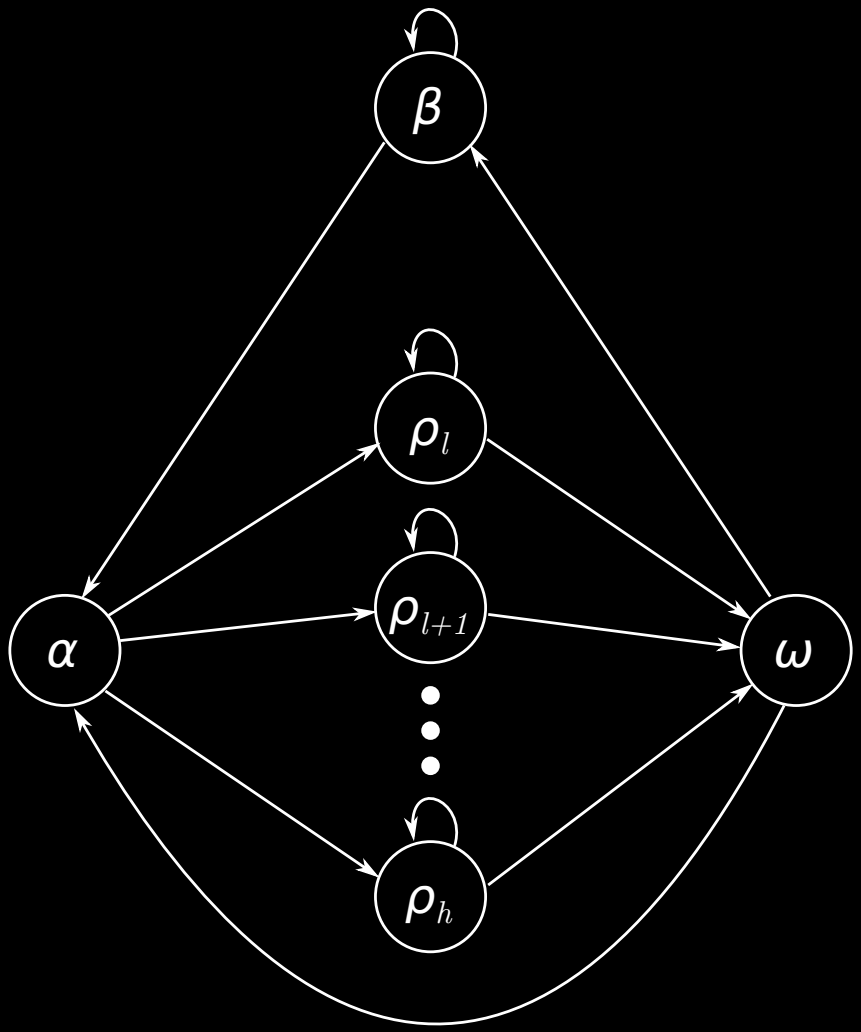
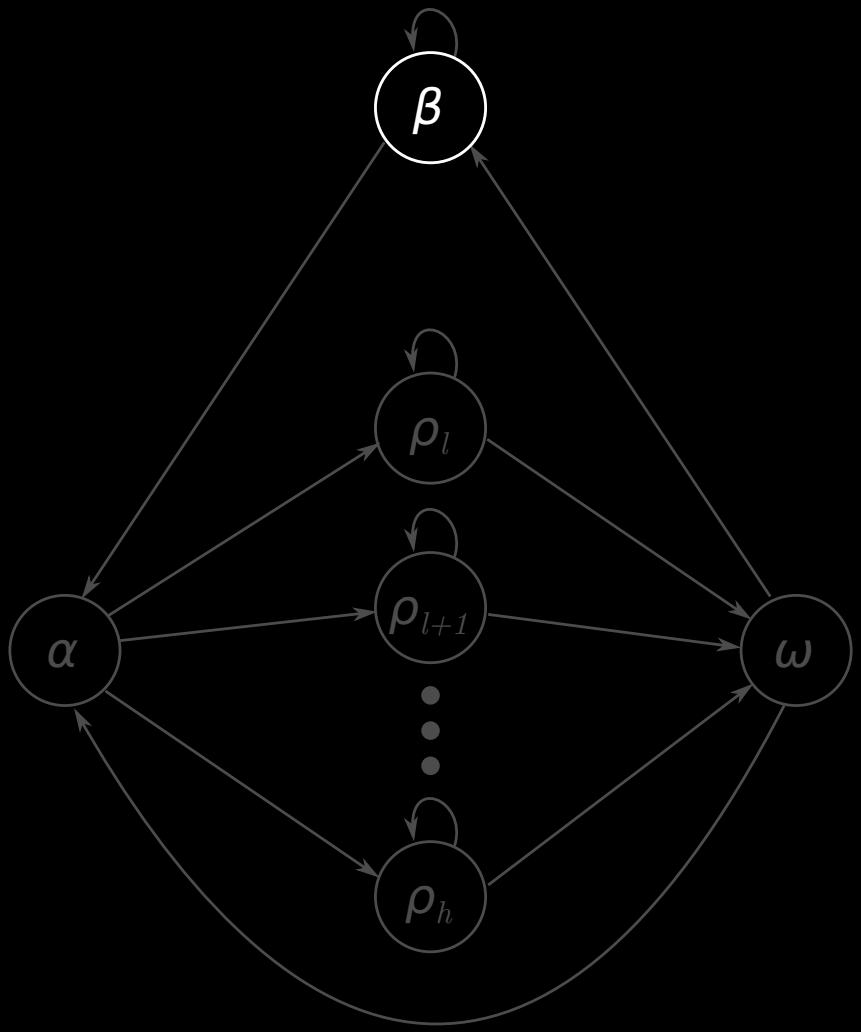
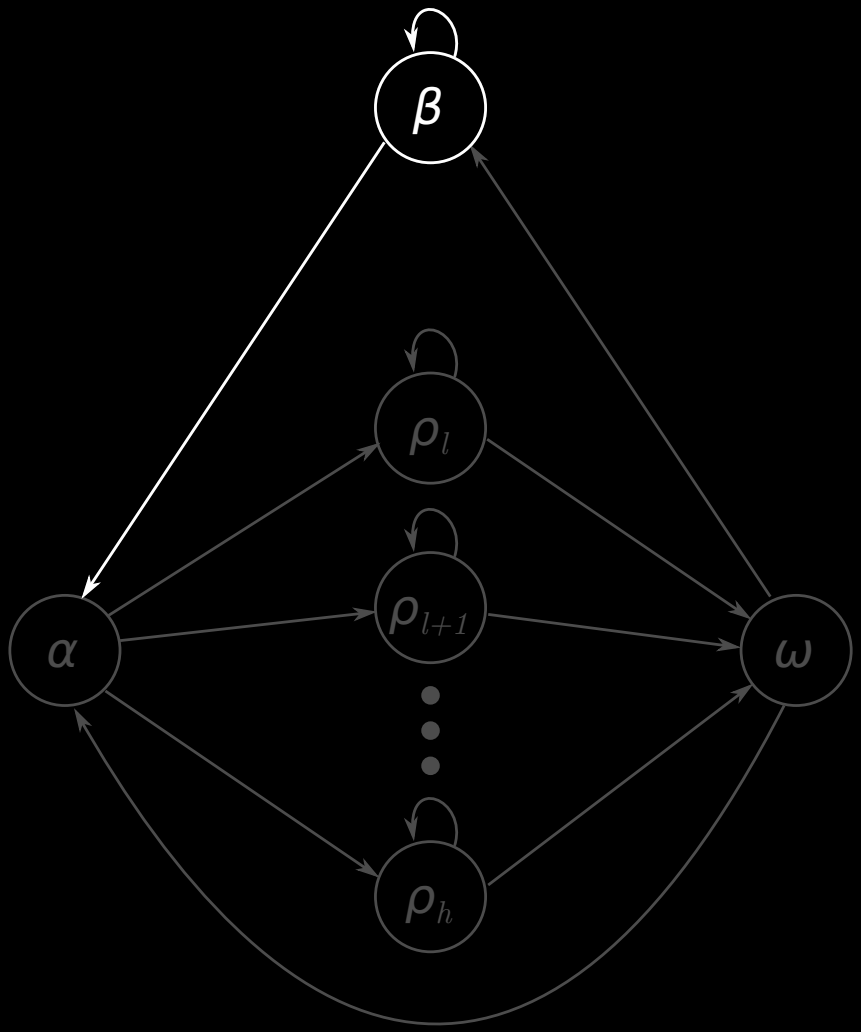


HMM pre nukleotidy



HMM pre nukleotidy



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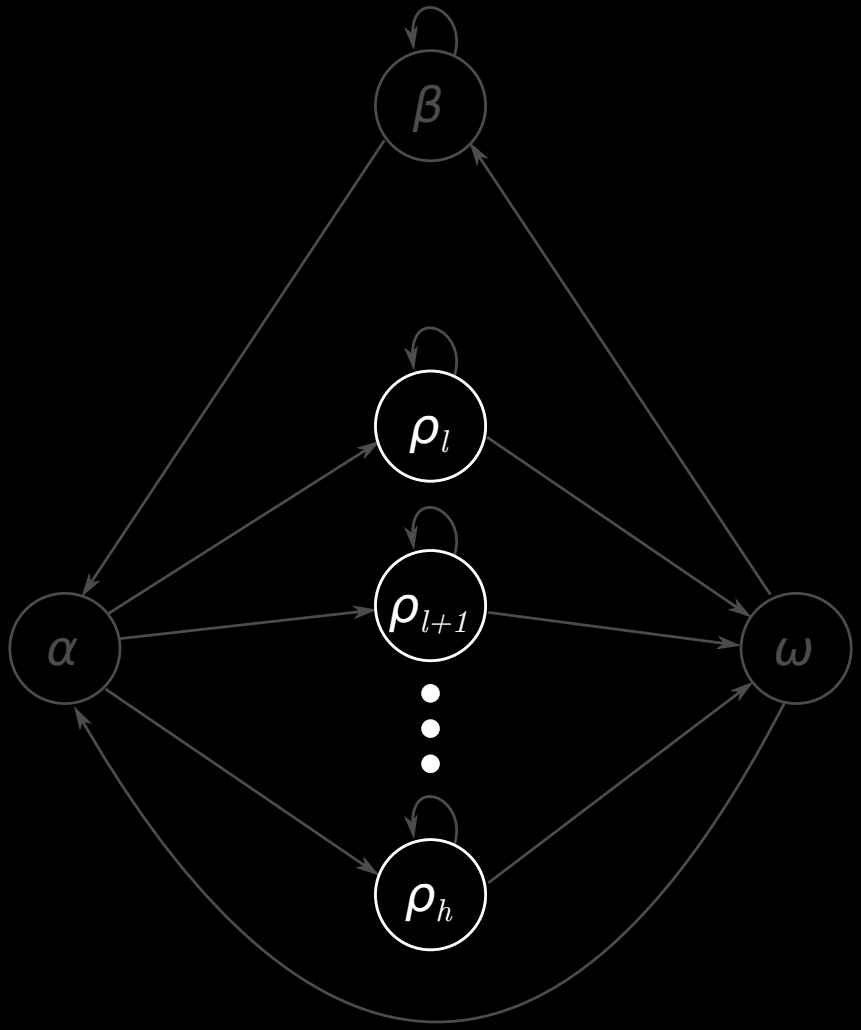

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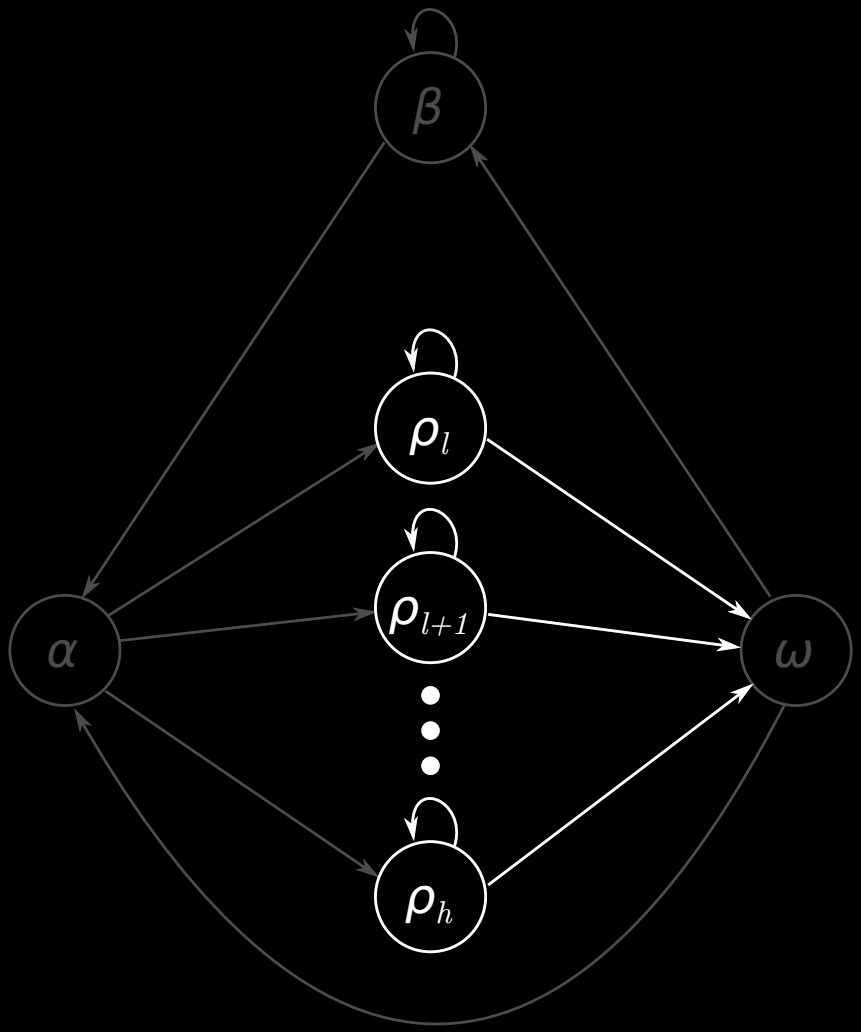
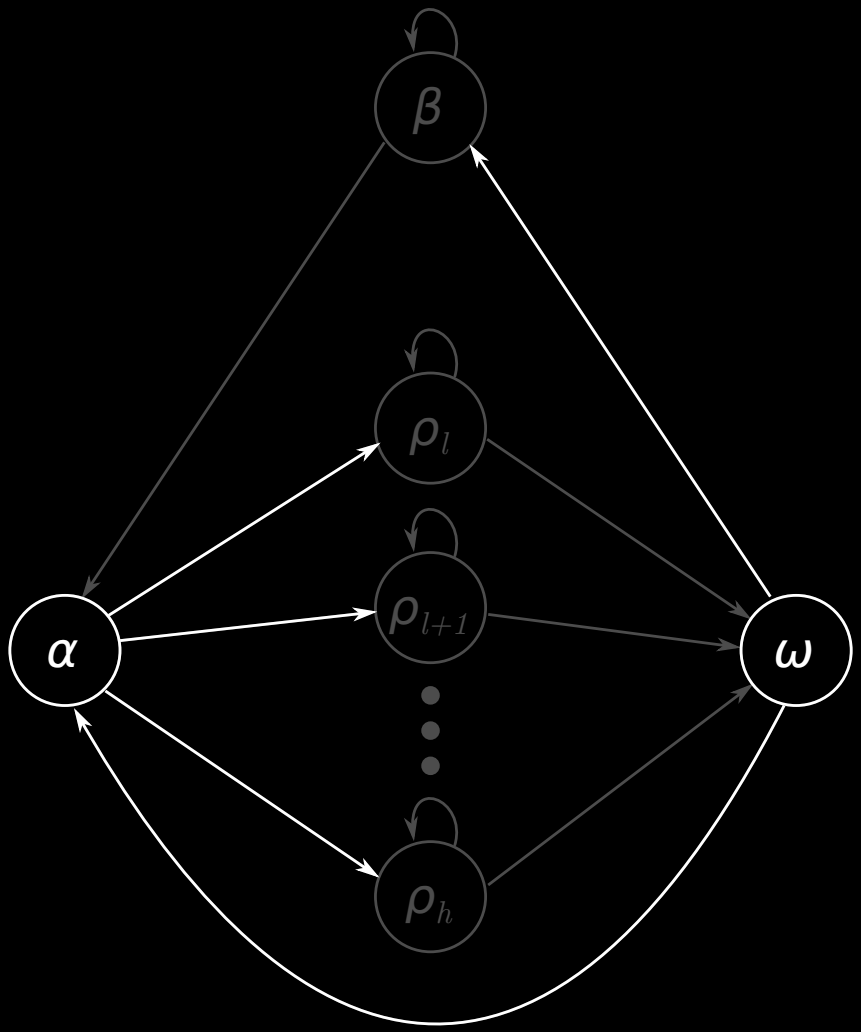
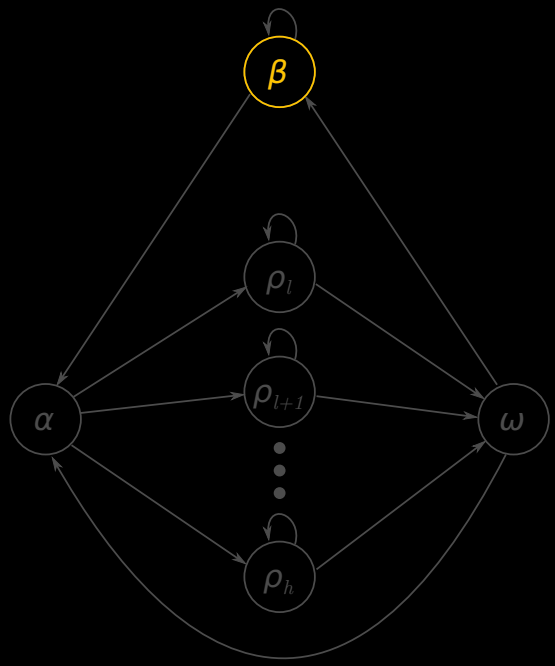


HMM pre nukleotidy



HMM pre nukleotidy

GGTCATCATCATCAA



HMM pre nukleotidy

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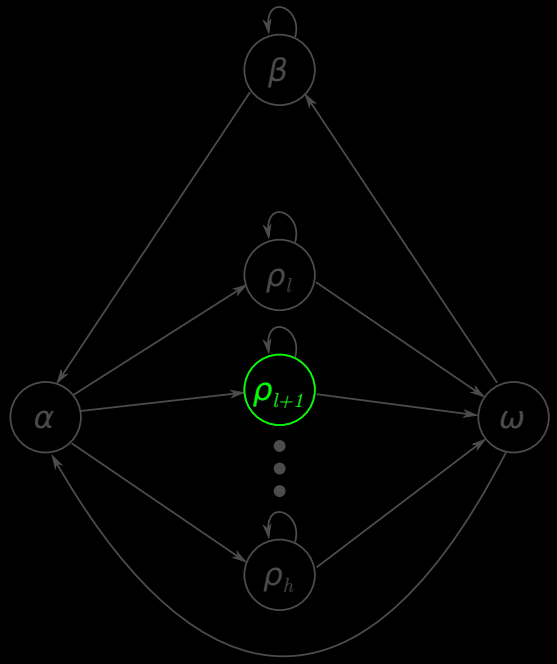

HMM pre nukleotidy

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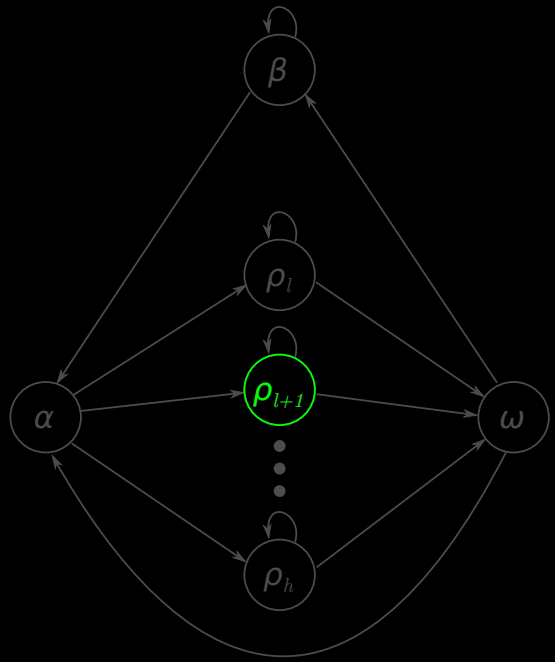

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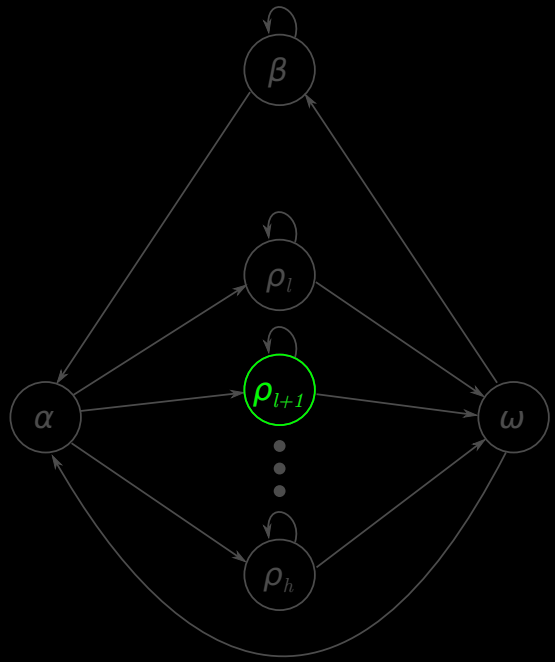

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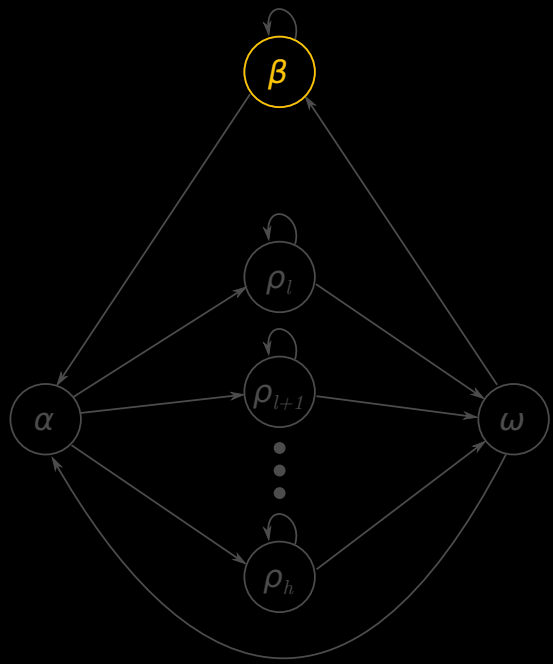
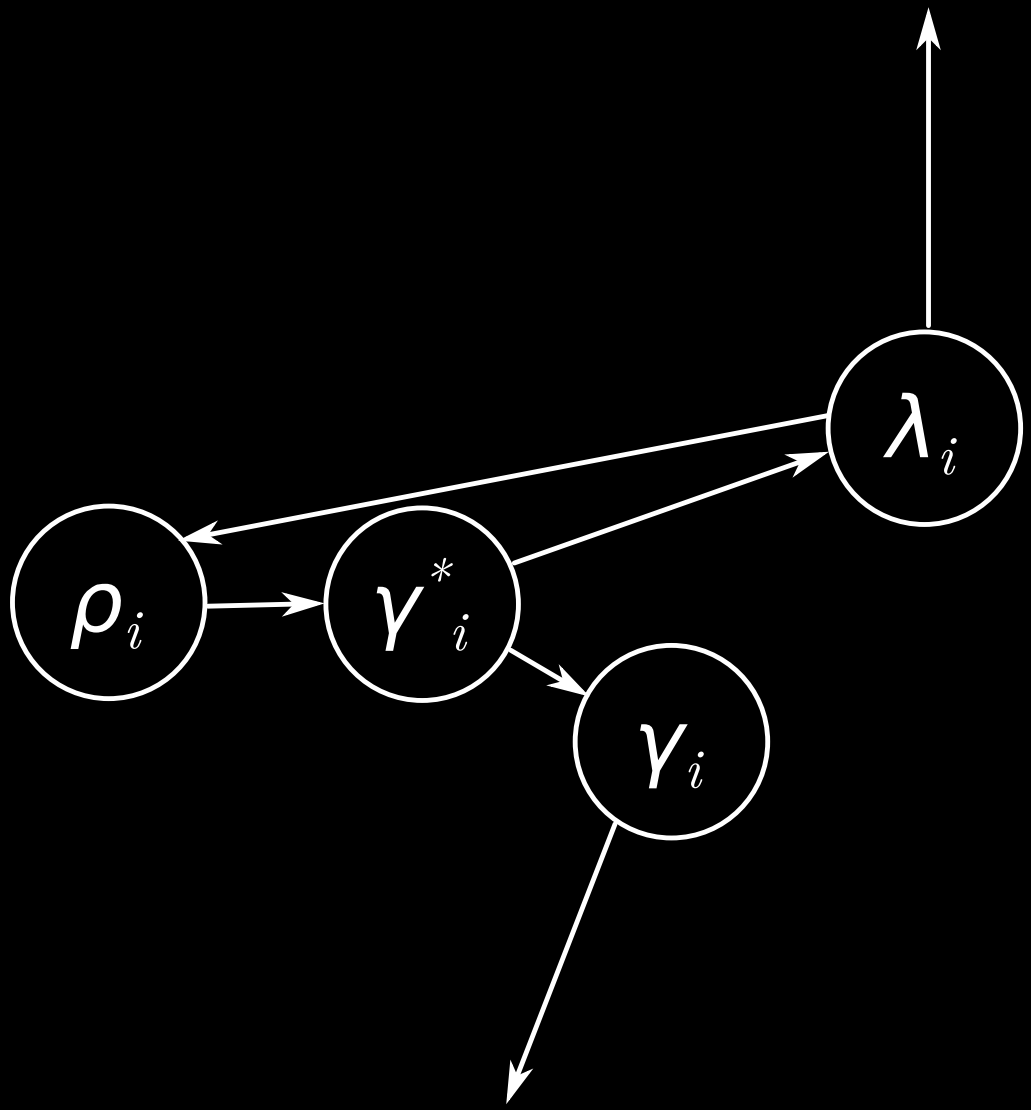


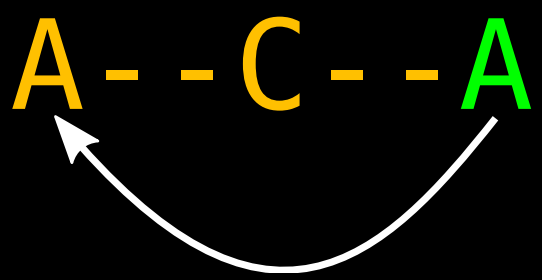
Rozširovanie HMM

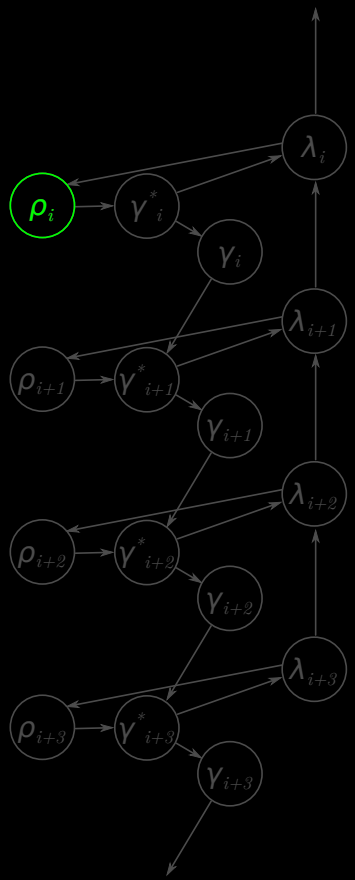
- HMM pre nukleotidy
- blanky
- nedokonalosti
- zlučovanie rovnakých označení

Blanky

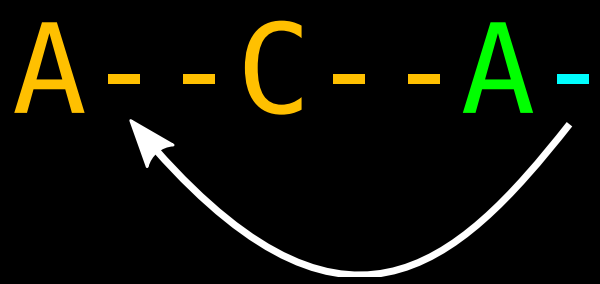


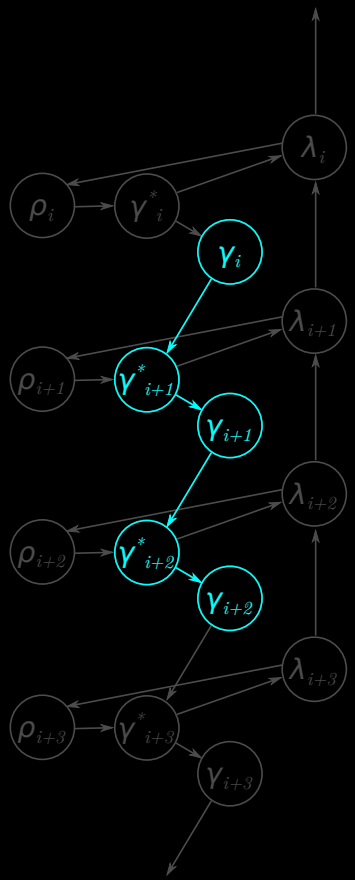
Blanky


A - - C - - A

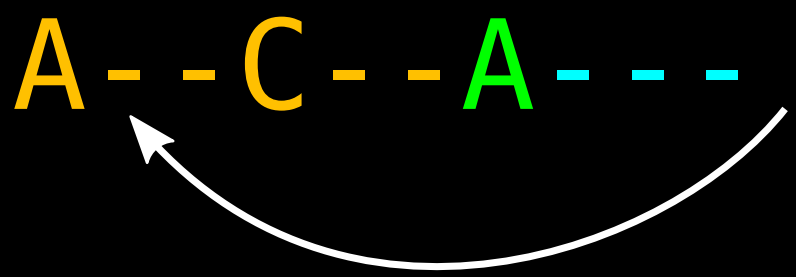

λ_i
ρ_i
γ^*_i
γ_i
λ_{i+1}
ρ_{i+1}
γ^*_{i+1}
γ_{i+1}
λ_{i+2}
ρ_{i+2}
γ^*_{i+2}
γ_{i+2}
λ_{i+3}
ρ_{i+3}
γ^*_{i+3}
γ_{i+3}

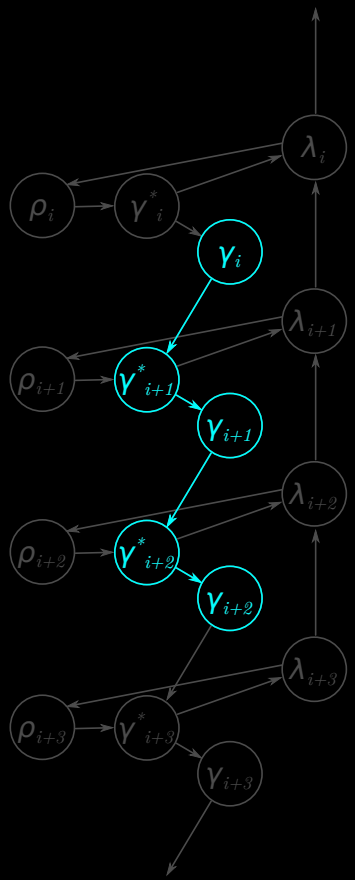
Blanky


A - - C - - A -

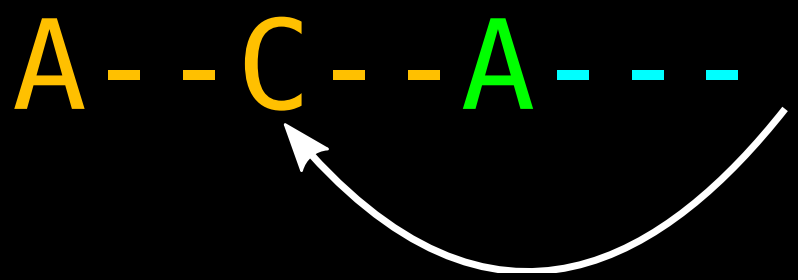

λ_i
ρ_i
γ^*_i
γ_i
λ_{i+1}
ρ_{i+1}
γ^*_{i+1}
γ_{i+1}
λ_{i+2}
ρ_{i+2}
γ^*_{i+2}
γ_{i+2}
λ_{i+3}
ρ_{i+3}
γ^*_{i+3}
γ_{i+3}

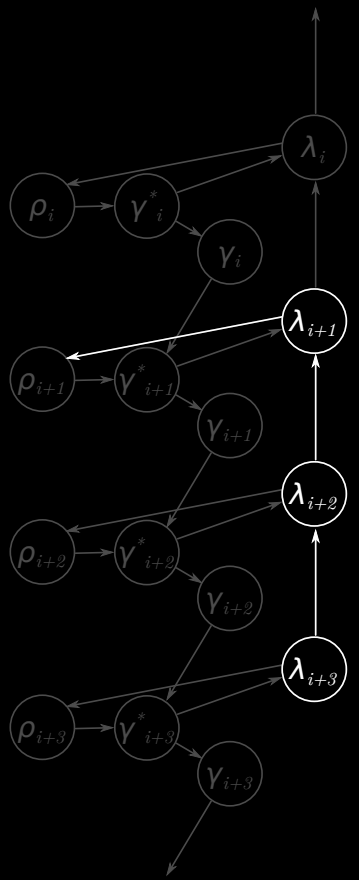
Blanky


A - - C - - A - - -


λ_i
ρ_i
γ^*_i
γ_i
λ_{i+1}
ρ_{i+1}
γ^*_{i+1}
γ_{i+1}
λ_{i+2}
ρ_{i+2}
γ^*_{i+2}
γ_{i+2}
λ_{i+3}
ρ_{i+3}
γ^*_{i+3}
γ_{i+3}

Blanky


A - - C - - A - - -


λ_i
ρ_i
γ^*_i
γ_i
λ_{i+1}
ρ_{i+1}
γ^*_{i+1}
γ_{i+1}
λ_{i+2}
ρ_{i+2}
γ^*_{i+2}
γ_{i+2}
λ_{i+3}
ρ_{i+3}
γ^*_{i+3}
γ_{i+3}

Rozširovanie HMM

- HMM pre nukleotidy
- blanky
- nedokonalosti
- zlučovanie rovnakých označení

Nedokonalosti

- zmenené nukleotidy
- emisná distribúcia v ρ
- inzercie
- emisná distribúcia v γ
- delécie
- prechody z λ

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Zlučovanie rovnakých označení

- modelovanie: zhruba 15-krát viac stavov
- ignorovanie: nižšia presnosť
- 

- Heuristika: lokálne maximá

Zlučovanie rovnakých označení

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Zlučovanie rovnakých označení

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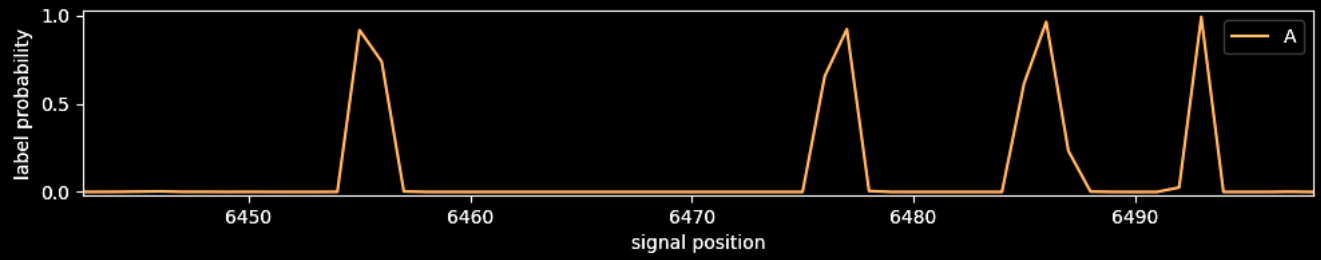

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Zlučovanie rovnakých označení

- modelovanie: zhruba 15-krát viac stavov
- ignorovanie: nižšia presnosť

- Heuristika: lokálne maximá

Vyhodnotenie

Datasety

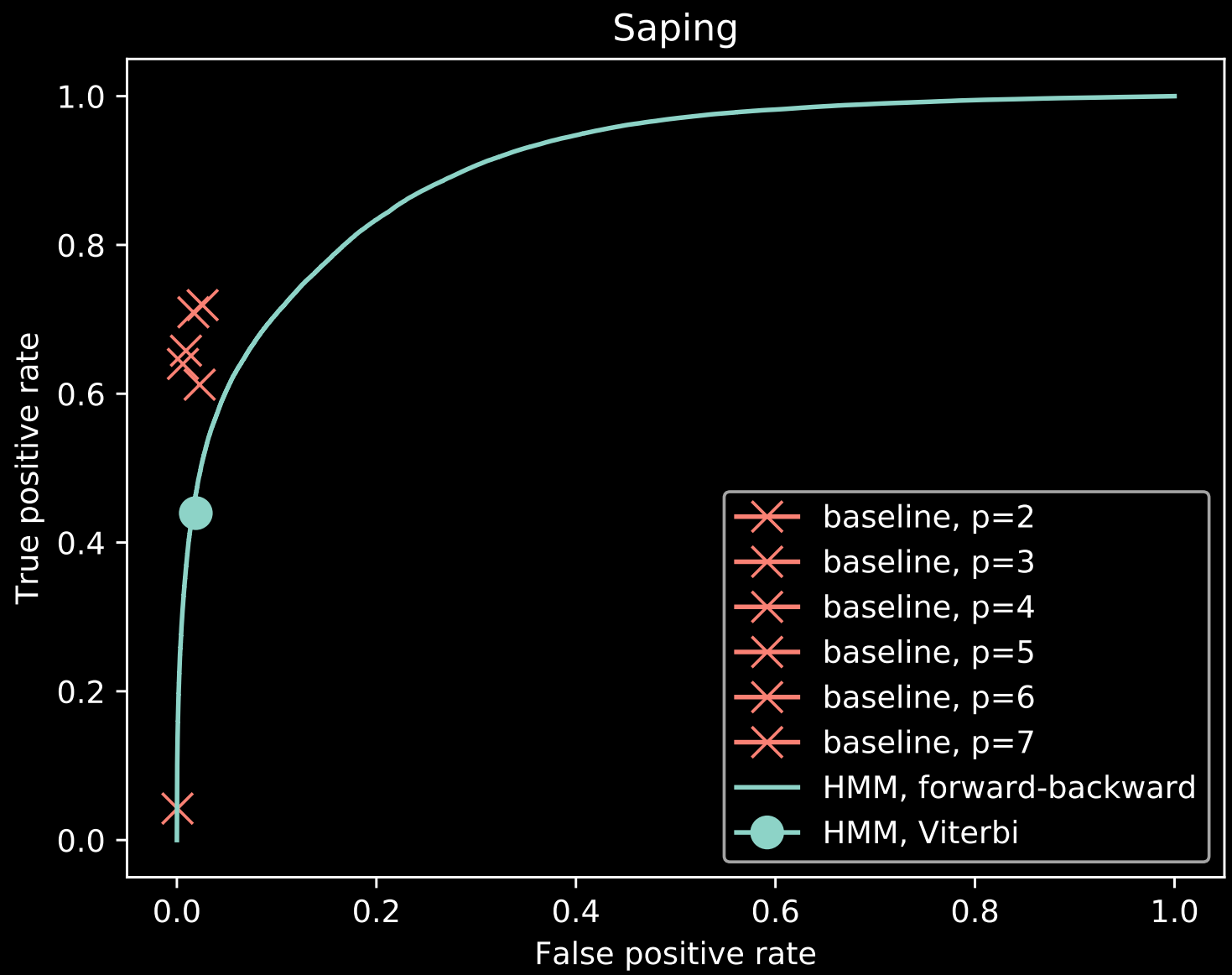
Name	**Reads**	**Repeats ratio**	**Average repeat period**
Saping	100	7.61%	5.84
Jamang	100	18.07%	63.72

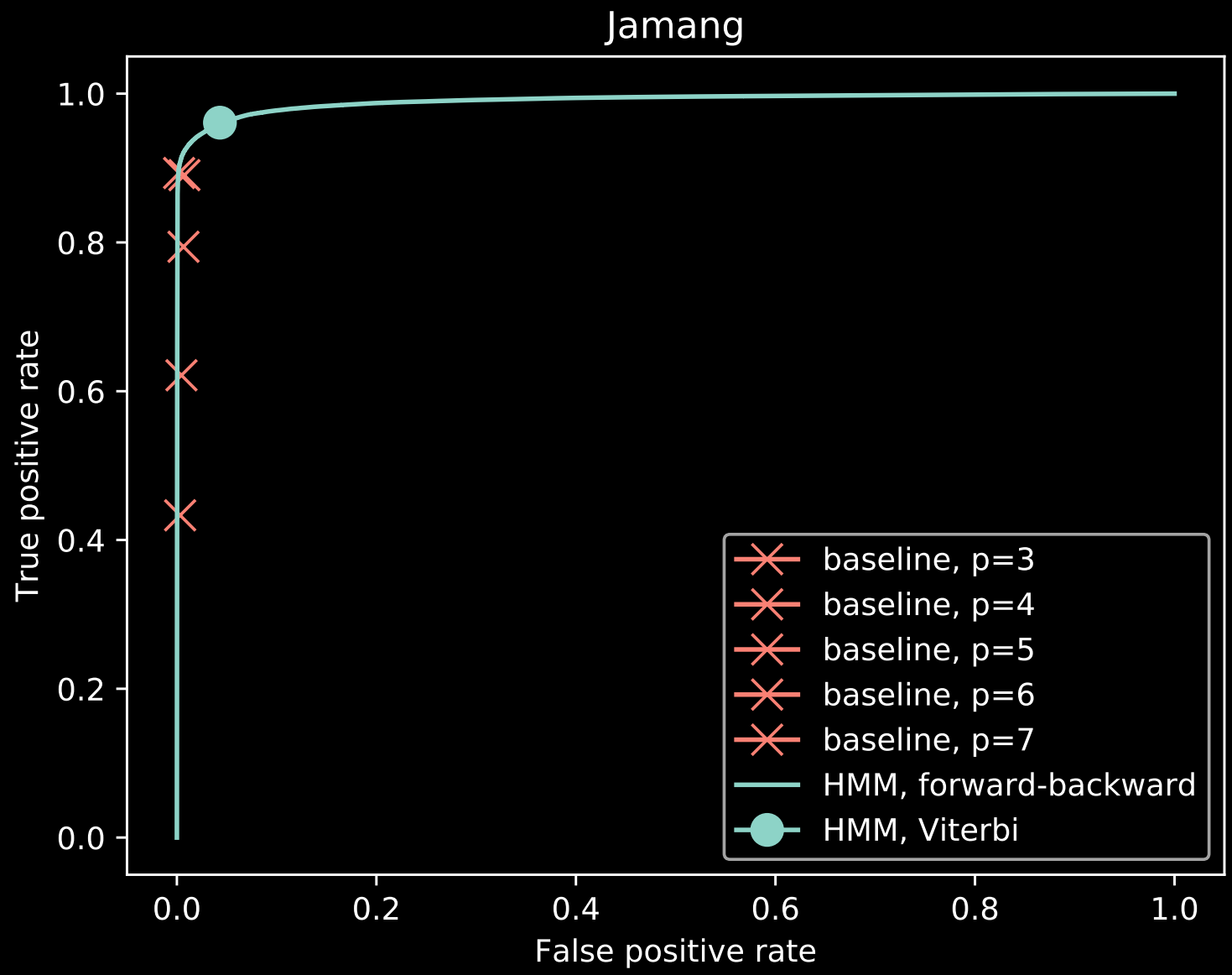
Metriky

- True positive rate
- False positive rate

Metriky

- True positive rate
- False positive rate


Saping
True positive rate
False positive rate
0.0
0.2
0.4
0.6
0.8
1.0
baseline, p=2
baseline, p=3
baseline, p=4
baseline, p=5
baseline, p=6
baseline, p=7
HMM, forward-backward
HMM, Viterbi


Jamang
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baseline, p=3
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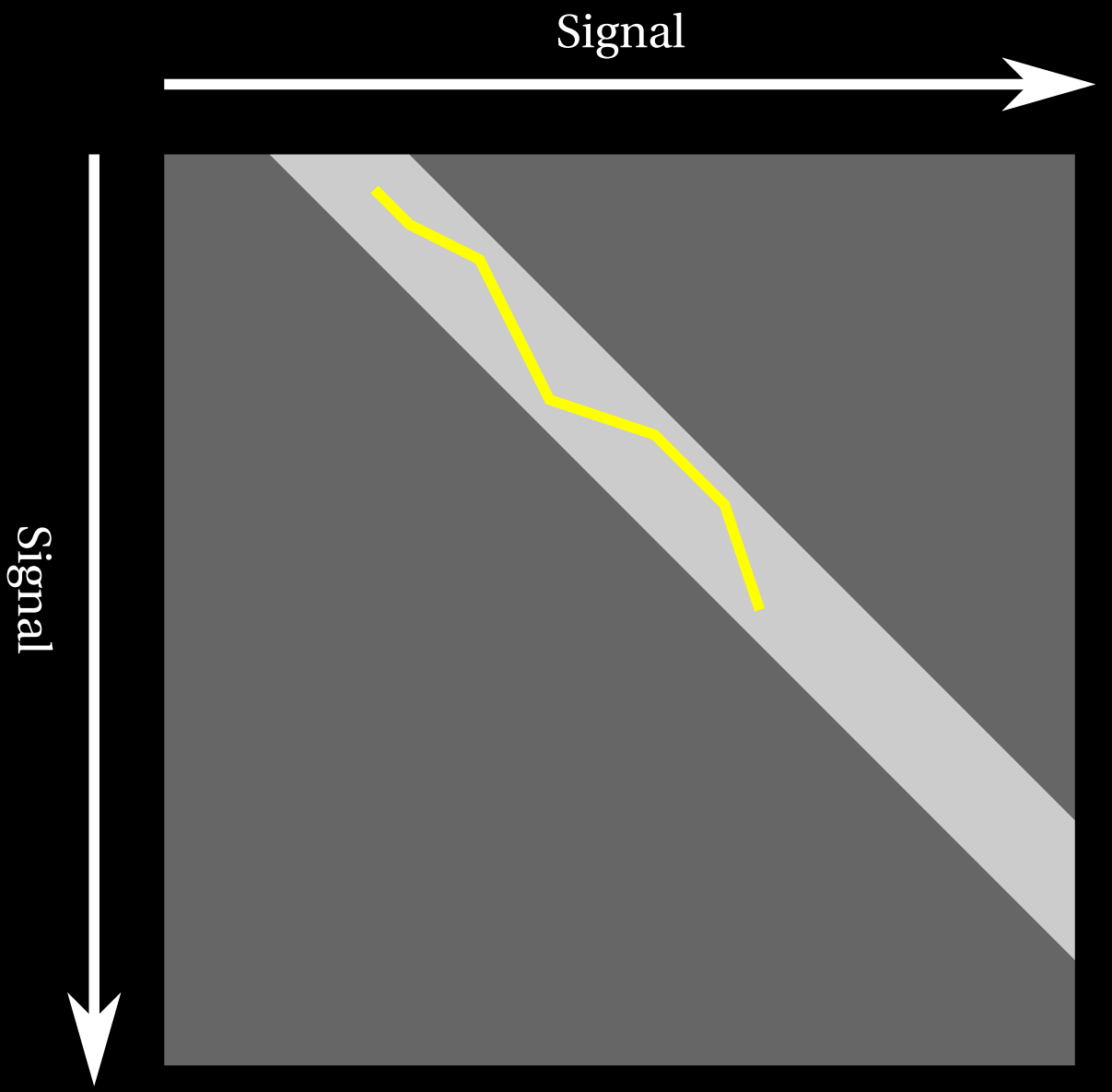
Použité obrázky

H. Teng et al. Chiron: translating nanopore raw signal directly into nucleotide sequence using deep learning. GigaScience, 7(5), 04 2018. giy037.

Otázka 1

- Akú funkciu optimalizuje algoritmus z kapitoly 3?
- Dala by sa upraviť tak, aby bolo možné použiť efektivnejší algoritmus?

Otázka 1



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Otázka 1

- $s_1 s_2 \ldots s_n$
- $t_1 t_2 \ldots t_m$
- $\begin{matrix} s_{i_1} & s_{i_2} & \ldots & s_{i_l} \\ t_{j_1} & t_{j_2} & \ldots & t_{j_l} \end{matrix}$
- $i_k \leq i_{k+1} \leq i_k + 1$
- $l \geq m, n$
- $\frac{b(n+m)}{2} - \sum_{k=1}^{l} (s_{i_k} - t_{i_k})^2$
- $b =$ bonus

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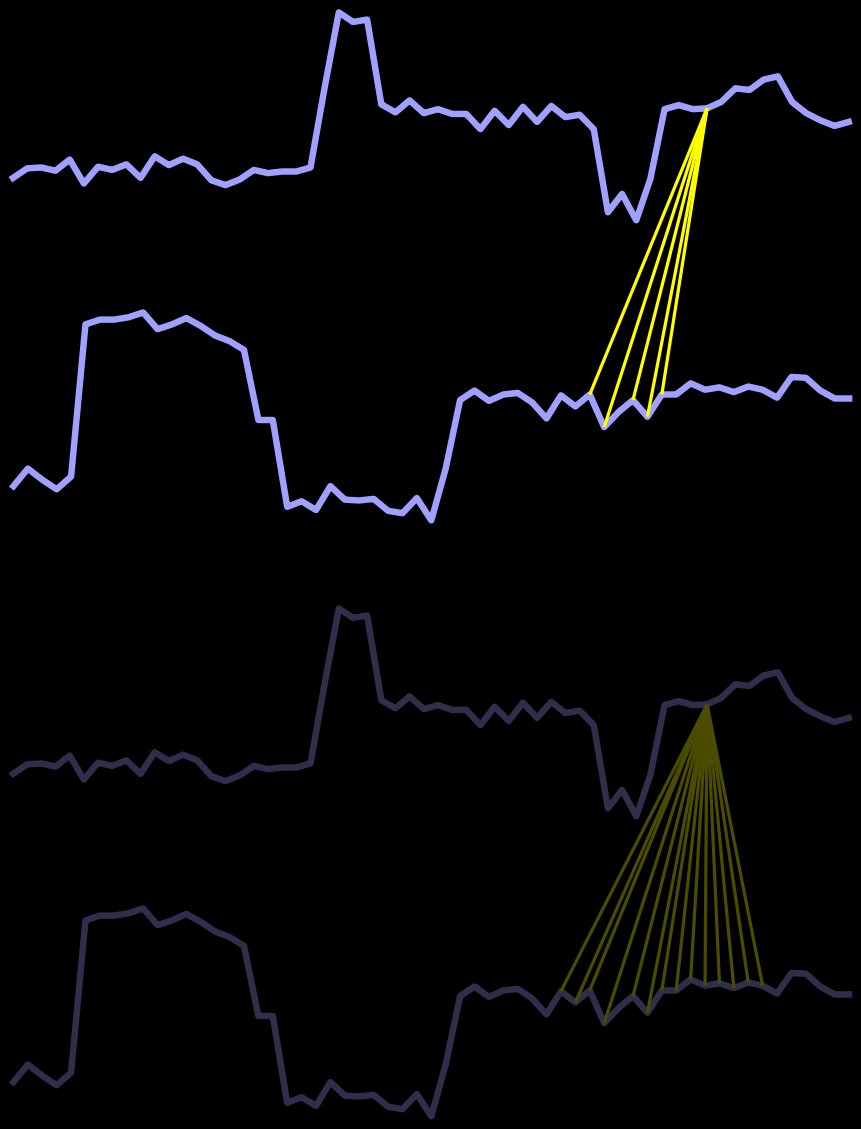

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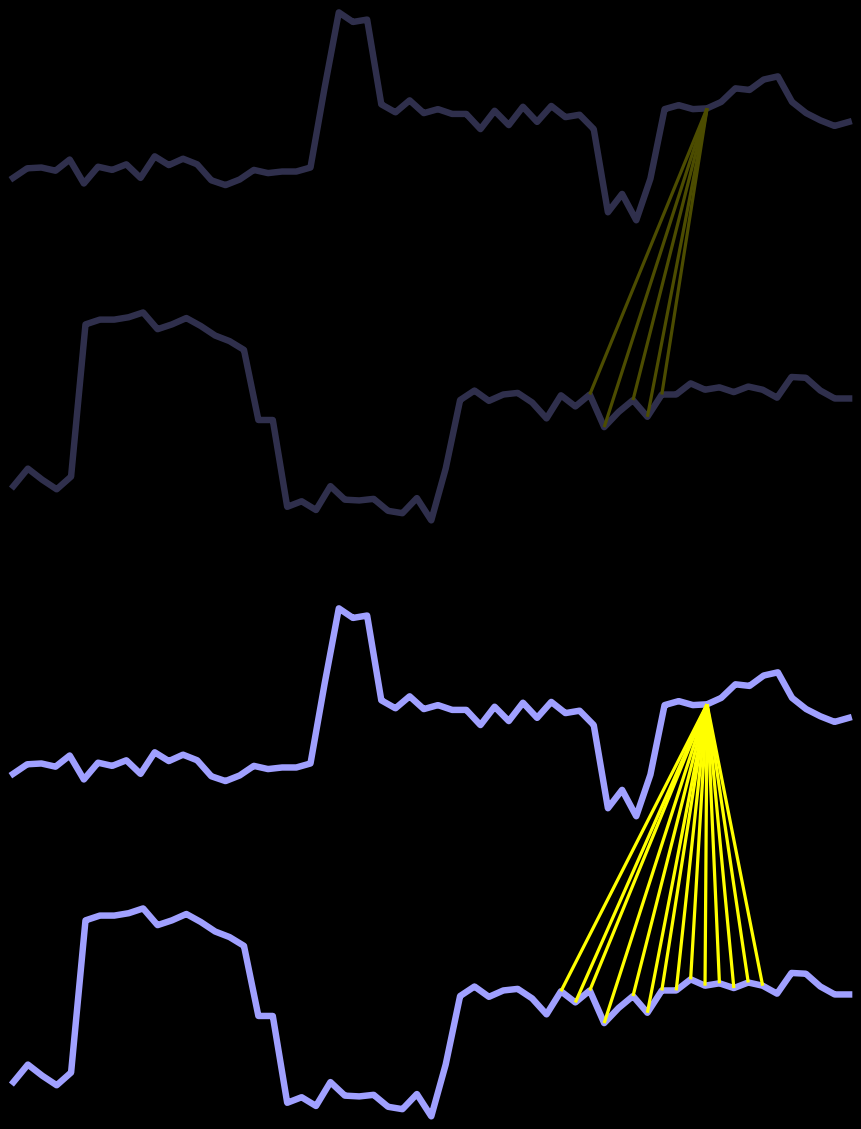

Otázka 2

- Alternatívny prístup z konca časti 4.2.5 s použitím preprocessovania a jednoduchého modelu nebol až tak horší ako plný model. Vedeli by ste si predstaviť presun ďalších častí plného modelu do preprocessingu? Ak áno, tak ktoré?
- Dal by sa tiež použiť algoritmus z kapitoly 3?

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