

Albert Einstein

# Eine neue Bestimmung der Moleküldimensionen

Diss. ETH No. ?



PESHO IVANOV

# SEQUENCE ALIGNMENT USING A\*



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SEQUENCE ALIGNMENT USING A\*

A dissertation submitted to attain the degree of

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presented by

PESHO IVANOV

Dipl., Eidgenössisches Polytechnikum

born on 14 March 1989

citizen of Bulgaria

accepted on the recommendation of

Prof. Dr. Martin Vechev, examiner

Prof. Dr. Gunnar Rätsch, co-examiner

Prof. Dr. Veli Mäkinen, co-examiner

Prof. Dr. Paul Medvedev, co-examiner

2022



To Vipassana





## ABSTRACT

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Sequence alignment is a class of problems aiming at unrevealing the relationship between sequences. These problems are of central interest in computational molecular biology for more than half a century and they are routinely applied in evolutionary biology, genome assembly, read mapping, variation detection and others.

Alignment algorithms involve a common tradeoff between optimality guarantees and performance. In this thesis, we consider a shortest path formulation of alignment and explore the application of the A\* algorithm. Most importantly, this approach enables us to design heuristic functions which combine optimality guarantees and polynomial speed ups.

Depending on the the number of aligned sequences, there is pairwise alignment and multiple sequence alignment (MSA). Depending on the parts of the sequences that are aligned to each other, we differentiate global, local and various semi-global alignments. There are generalizations to sequence-to-sequence alignment, including aligning to nonlinear structures, such as directed acyclic graphs, DAGs, general graphs and others. These structures are nowadays becoming more present as a compressed form of representing a set of references to which a sequence can be aligned. Often, one best alignment is sufficient but finding several best (top-K) alignments.

The number of possible alignments grow exponentially with length. The usual underlying question to finding “correct” alignments. Regarding the precision of alignment, one is usually interested in base-to-base (aka letter-to-letter) correspondence between the sequences, even though for some applications a less detailed solution is sufficient: only the similarity between sequences or the location where a read maps to a reference. Exact alignment is only useful for very short sequences (often kmers), and for all other cases the optimized metric may be hamming distance, edit distance (unit costs), Levenshtein distance, affine costs, convex and concave costs, general costs and others.

The classical dynamic solutions are the so called Needleman-Wunsch. Currently, researchers still face the In the context of read mapping, a set of reads is aligned to the same reference sequence so an indexing procedure is often useful for the performance.

A good algorithm should be optimal, complete, performant (fast and low on memory) on short and long sequences, various error rates and error models, and reference complexity (topology and entropy).

Many tools do not have a well-stated problem they optimize.

Probabilistic approach.

## ZUSAMMENFASSUNG

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Deutsche Zusammenfassung hier.



## ACKNOWLEDGEMENTS

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I would like to thank ...



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## NOTATION

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### FREQUENTLY USED SYMBOLS

$E$  energy

$m$  rest mass

$p$  impulse

### PHYSICAL CONSTANTS

$c$  speed of light in vacuum,  $c = 299\,792\,458\,\text{m s}^{-1}$

(CODATA 2014 [1])



## INTRODUCTION

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*Sapere aude! Habe Mut, dich deines eigenen  
Verstandes zu bedienen!*

— Immanuel Kant

Die ältesten Bestimmungen der wahren Grösse der Moleküle hat die kinetische Theorie der Gase ermöglicht, während die an Flüssigkeiten beobachteten physikalischen Phänomene bis jetzt zur Bestimmung der Molekülgrössen nicht gedient haben. ...



## SAMPLE CHAPTER

*The true logic of this world is in the calculus of probabilities.*

— James C. Maxwell

Maxwell [2] derived some very useful equations for electromagnetic fields:

$$\nabla \cdot \vec{D} = \rho \quad (2.1)$$

$$\nabla \cdot \vec{B} = 0 \quad (2.2)$$

$$\nabla \times \vec{E} = -\frac{\partial \vec{B}}{\partial t} \quad (2.3)$$

$$\nabla \times \vec{H} = \vec{j} + \frac{\partial \vec{D}}{\partial t} \quad (2.4)$$

The energy–momentum relation, eq. (2.5), is one of *my* important results:

$$E^2 = m^2 c^4 + (pc)^2 \quad (2.5)$$

Write units like this: 5  $\mu\text{m}$ .

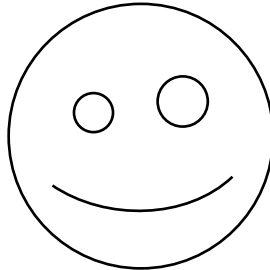


FIGURE 2.1: A lovely face.



## HEADING ON LEVEL 0 (CHAPTER)

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Hello, here is some text without a meaning. This text should show what a printed text will look like at this place. If you read this text, you will get no information. Really? Is there no information? Is there a difference between this text and some nonsense like “Huardest gefburn”? Kjift – not at all! A blind text like this gives you information about the selected font, how the letters are written and an impression of the look. This text should contain all letters of the alphabet and it should be written in of the original language. There is no need for special content, but the length of words should match the language.

### 3.1 HEADING ON LEVEL 1 (SECTION)

Hello, here is some text without a meaning. This text should show what a printed text will look like at this place. If you read this text, you will get no information. Really? Is there no information? Is there a difference between this text and some nonsense like “Huardest gefburn”? Kjift – not at all! A blind text like this gives you information about the selected font, how the letters are written and an impression of the look. This text should contain all letters of the alphabet and it should be written in of the original language. There is no need for special content, but the length of words should match the language.

This is the second paragraph. Hello, here is some text without a meaning. This text should show what a printed text will look like at this place. If you read this text, you will get no information. Really? Is there no information? Is there a difference between this text and some nonsense like “Huardest gefburn”? Kjift – not at all! A blind text like this gives you information about the selected font, how the letters are written and an impression of the look. This text should contain all letters of the alphabet and it should be written in of the original language. There is no need for special content, but the length of words should match the language.

And after the second paragraph follows the third paragraph. Hello, here is some text without a meaning. This text should show what a printed text will look like at this place. If you read this text, you will get no information.

Really? Is there no information? Is there a difference between this text and some nonsense like “Huardest gefburn”? Kjift – not at all! A blind text like this gives you information about the selected font, how the letters are written and an impression of the look. This text should contain all letters of the alphabet and it should be written in of the original language. There is no need for special content, but the length of words should match the language.

After this fourth paragraph, we start a new paragraph sequence. Hello, here is some text without a meaning. This text should show what a printed text will look like at this place. If you read this text, you will get no information. Really? Is there no information? Is there a difference between this text and some nonsense like “Huardest gefburn”? Kjift – not at all! A blind text like this gives you information about the selected font, how the letters are written and an impression of the look. This text should contain all letters of the alphabet and it should be written in of the original language. There is no need for special content, but the length of words should match the language.

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### 3.1.1 *Heading on Level 2 (subsection)*

This is the second paragraph. Hello, here is some text without a meaning. This text should show what a printed text will look like at this place. If you read this text, you will get no information. Really? Is there no information? Is there a difference between this text and some nonsense like “Huardest gefburn”? Kjift – not at all! A blind text like this gives you information about the selected font, how the letters are written and an impression of the look. This text should contain all letters of the alphabet and it should be written in of the original language. There is no need for special content, but the length of words should match the language.

And after the second paragraph follows the third paragraph. Hello, here is some text without a meaning. This text should show what a printed text will look like at this place. If you read this text, you will get no information. Really? Is there no information? Is there a difference between this text and some nonsense like “Huardest gefburn”? Kjift – not at all! A blind text like this gives you information about the selected font, how the letters are written and an impression of the look. This text should contain all letters of the alphabet and it should be written in of the original language. There is no need for special content, but the length of words should match the language.

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### 3.1.1.1 *Heading on Level 3 (subsection)*

And after the second paragraph follows the third paragraph. Hello, here is some text without a meaning. This text should show what a printed text will look like at this place. If you read this text, you will get no information. Really? Is there no information? Is there a difference between this text and some nonsense like “Huardest gefburn”? Kjift – not at all! A blind text like this gives you information about the selected font, how the letters are written and an impression of the look. This text should contain all letters of the alphabet and it should be written in of the original language. There is no need for special content, but the length of words should match the language.

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HEADING ON LEVEL 4 (PARAGRAPH) After this fourth paragraph, we start a new paragraph sequence. Hello, here is some text without a meaning. This text should show what a printed text will look like at this place. If you read this text, you will get no information. Really? Is there no information? Is there a difference between this text and some nonsense like “Huardest gefburn”? Kjift – not at all! A blind text like this gives you information about the selected font, how the letters are written and an impression of the look. This text should contain all letters of the alphabet and it should be written in of the original language. There is no need for special content, but the length of words should match the language.

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## 3.2    LISTS

### 3.2.1   *Example for list (itemize)*

- Hello, here is some text without a meaning. This text should show what a printed text will look like at this place. If you read this text, you will get no information. Really? Is there no information? Is there a difference between this text and some nonsense like “Huardest gefburn”? Kjift – not at all! A blind text like this gives you information about the selected font, how the letters are written and an impression of the look. This text should contain all letters of the alphabet and it should be written in of the original language. There is no need for special content, but the length of words should match the language.
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#### 3.2.1.1 Example for list (4\*itemize)

- Hello, here is some text without a meaning. This text should show what a printed text will look like at this place. If you read this text, you will get no information. Really? Is there no information? Is there a difference between this text and some nonsense like “Huardest

gefburn"? Kjift – not at all! A blind text like this gives you information about the selected font, how the letters are written and an impression of the look. This text should contain all letters of the alphabet and it should be written in of the original language. There is no need for special content, but the length of words should match the language.

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of the look. This text should contain all letters of the alphabet and it should be written in of the original language. There is no need for special content, but the length of words should match the language.

### 3.2.2 *Example for list (enumerate)*

1. Hello, here is some text without a meaning. This text should show what a printed text will look like at this place. If you read this text, you will get no information. Really? Is there no information? Is there a difference between this text and some nonsense like “Huardest gefburn”? Kjift – not at all! A blind text like this gives you information about the selected font, how the letters are written and an impression of the look. This text should contain all letters of the alphabet and it should be written in of the original language. There is no need for special content, but the length of words should match the language.
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about the selected font, how the letters are written and an impression of the look. This text should contain all letters of the alphabet and it should be written in of the original language. There is no need for special content, but the length of words should match the language.

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#### 3.2.2.1 *Example for list (q\*enumerate)*

1. Hello, here is some text without a meaning. This text should show what a printed text will look like at this place. If you read this text, you will get no information. Really? Is there no information? Is there a difference between this text and some nonsense like “Huardest gefburn”? Kjift – not at all! A blind text like this gives you information about the selected font, how the letters are written and an impression of the look. This text should contain all letters of the alphabet and it should be written in of the original language. There is no need for special content, but the length of words should match the language.
  - a) Hello, here is some text without a meaning. This text should show what a printed text will look like at this place. If you read this text, you will get no information. Really? Is there no information? Is there a difference between this text and some nonsense like “Huardest gefburn”? Kjift – not at all! A blind text like this gives you information about the selected font, how the letters are written and an impression of the look. This text should contain all letters of the alphabet and it should be written in of the original language. There is no need for special content, but the length of words should match the language.
    - i. Hello, here is some text without a meaning. This text should show what a printed text will look like at this place. If you read this text, you will get no information. Really? Is there no information? Is there a difference between this text and

some nonsense like “Huardest gefburn”? Kjift – not at all! A blind text like this gives you information about the selected font, how the letters are written and an impression of the look. This text should contain all letters of the alphabet and it should be written in of the original language. There is no need for special content, but the length of words should match the language.

- A. Hello, here is some text without a meaning. This text should show what a printed text will look like at this place. If you read this text, you will get no information. Really? Is there no information? Is there a difference between this text and some nonsense like “Huardest gefburn”? Kjift – not at all! A blind text like this gives you information about the selected font, how the letters are written and an impression of the look. This text should contain all letters of the alphabet and it should be written in of the original language. There is no need for special content, but the length of words should match the language.
- B. Hello, here is some text without a meaning. This text should show what a printed text will look like at this place. If you read this text, you will get no information. Really? Is there no information? Is there a difference between this text and some nonsense like “Huardest gefburn”? Kjift – not at all! A blind text like this gives you information about the selected font, how the letters are written and an impression of the look. This text should contain all letters of the alphabet and it should be written in of the original language. There is no need for special content, but the length of words should match the language.
- ii. Hello, here is some text without a meaning. This text should show what a printed text will look like at this place. If you read this text, you will get no information. Really? Is there no information? Is there a difference between this text and some nonsense like “Huardest gefburn”? Kjift – not at all! A blind text like this gives you information about the selected font, how the letters are written and an impression of the look. This text should contain all letters of the alphabet and



it should be written in of the original language. There is no need for special content, but the length of words should match the language.

- b) Hello, here is some text without a meaning. This text should show what a printed text will look like at this place. If you read this text, you will get no information. Really? Is there no information? Is there a difference between this text and some nonsense like “Huardest gefburn”? Kjift – not at all! A blind text like this gives you information about the selected font, how the letters are written and an impression of the look. This text should contain all letters of the alphabet and it should be written in of the original language. There is no need for special content, but the length of words should match the language.
2. Hello, here is some text without a meaning. This text should show what a printed text will look like at this place. If you read this text, you will get no information. Really? Is there no information? Is there a difference between this text and some nonsense like “Huardest gefburn”? Kjift – not at all! A blind text like this gives you information about the selected font, how the letters are written and an impression of the look. This text should contain all letters of the alphabet and it should be written in of the original language. There is no need for special content, but the length of words should match the language.

### 3.2.3 *Example for list (description)*

FIRST ITEM IN A LIST Hello, here is some text without a meaning. This text should show what a printed text will look like at this place. If you read this text, you will get no information. Really? Is there no information? Is there a difference between this text and some nonsense like “Huardest gefburn”? Kjift – not at all! A blind text like this gives you information about the selected font, how the letters are written and an impression of the look. This text should contain all letters of the alphabet and it should be written in of the original language. There is no need for special content, but the length of words should match the language.

SECOND ITEM IN A LIST Hello, here is some text without a meaning. This text should show what a printed text will look like at this place. If you read this text, you will get no information. Really? Is there no

information? Is there a difference between this text and some nonsense like “Huardest gefburn”? Kjift – not at all! A blind text like this gives you information about the selected font, how the letters are written and an impression of the look. This text should contain all letters of the alphabet and it should be written in of the original language. There is no need for special content, but the length of words should match the language.

THIRD ITEM IN A LIST Hello, here is some text without a meaning. This text should show what a printed text will look like at this place. If you read this text, you will get no information. Really? Is there no information? Is there a difference between this text and some nonsense like “Huardest gefburn”? Kjift – not at all! A blind text like this gives you information about the selected font, how the letters are written and an impression of the look. This text should contain all letters of the alphabet and it should be written in of the original language. There is no need for special content, but the length of words should match the language.

FOURTH ITEM IN A LIST Hello, here is some text without a meaning. This text should show what a printed text will look like at this place. If you read this text, you will get no information. Really? Is there no information? Is there a difference between this text and some nonsense like “Huardest gefburn”? Kjift – not at all! A blind text like this gives you information about the selected font, how the letters are written and an impression of the look. This text should contain all letters of the alphabet and it should be written in of the original language. There is no need for special content, but the length of words should match the language.

FIFTH ITEM IN A LIST Hello, here is some text without a meaning. This text should show what a printed text will look like at this place. If you read this text, you will get no information. Really? Is there no information? Is there a difference between this text and some nonsense like “Huardest gefburn”? Kjift – not at all! A blind text like this gives you information about the selected font, how the letters are written and an impression of the look. This text should contain all letters of the alphabet and it should be written in of the original language. There is no need for special content, but the length of words should match the language.

### 3.2.3.1 *Example for list (q\*description)*

FIRST ITEM IN A LIST Hello, here is some text without a meaning. This text should show what a printed text will look like at this place. If you read this text, you will get no information. Really? Is there no information? Is there a difference between this text and some nonsense like “Huardest gefburn”? Kjift – not at all! A blind text like this gives you information about the selected font, how the letters are written and an impression of the look. This text should contain all letters of the alphabet and it should be written in of the original language. There is no need for special content, but the length of words should match the language.

FIRST ITEM IN A LIST Hello, here is some text without a meaning. This text should show what a printed text will look like at this place. If you read this text, you will get no information. Really? Is there no information? Is there a difference between this text and some nonsense like “Huardest gefburn”? Kjift – not at all! A blind text like this gives you information about the selected font, how the letters are written and an impression of the look. This text should contain all letters of the alphabet and it should be written in of the original language. There is no need for special content, but the length of words should match the language.

FIRST ITEM IN A LIST Hello, here is some text without a meaning. This text should show what a printed text will look like at this place. If you read this text, you will get no information. Really? Is there no information? Is there a difference between this text and some nonsense like “Huardest gefburn”? Kjift – not at all! A blind text like this gives you information about the selected font, how the letters are written and an impression of the look. This text should contain all letters of the alphabet and it should be written in of the original language. There is no need for special content, but the length of words should match the language.

FIRST ITEM IN A LIST Hello, here is some text without a meaning. This text should show what a printed text will look like at this place. If you read this text, you will get no information. Really? Is there no information? Is there a difference between this text and some nonsense like “Huardest gefburn”? Kjift – not at all! A blind text like

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SECOND ITEM IN A LIST Hello, here is some text without a meaning. This text should show what a printed text will look like at this place. If you read this text, you will get no information. Really? Is there no information? Is there a difference between this text and some nonsense like “Huardest gefburn”? Kjift – not at all! A blind text like this gives you information about the selected font, how the letters are written and an impression of the look. This text should contain all letters of the alphabet and it should be written in of the original language. There is no need for special content, but the length of words should match the language.

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SECOND ITEM IN A LIST Hello, here is some text without a meaning. This text should show what a printed text will look like at this place. If you read this text, you will get no information. Really? Is there no information? Is there a difference between this text and some nonsense like “Huardest gefburn”? Kjift – not at all! A blind text like this gives you information about the selected font, how the letters are written and an impression of the look. This text should contain all letters of the alphabet and it should be written in of the original language. There is no need for special content, but the length of words should match the language.

SECOND ITEM IN A LIST Hello, here is some text without a meaning. This text should show what a printed text will look like at this place. If you read this text, you will get no information. Really? Is there no information? Is there a difference between this text and some nonsense like “Huardest gefburn”? Kjift – not at all! A blind text like this gives you information about the selected font, how the letters are written and an impression of the look. This text should contain all letters of the alphabet and it should be written in of the original language. There is no need for special content, but the length of words should match the language.



SUMMARY

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*I dream my painting and I paint my dream.*

— Vincent van Gogh

Summary here.







## APPENDIX

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Here be dragons.



## BIBLIOGRAPHY

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## CURRICULUM VITAE

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### PERSONAL DATA

Name	Albert Einstein
Date of Birth	March 14, 1879
Place of Birth	Ulm, Germany
Citizen of	Switzerland

### EDUCATION

1896 – 1900	Eidgenössisches Polytechnikum, Zürich, Switzerland <i>Final degree:</i> Diploma
1895 – 1896	Aargauische Kantonsschule (grammar school) Aarau, Switzerland <i>Final degree:</i> Matura (university entrance diploma)
– July 1894	Luitpold-Gymnasium (grammar school) Munich, Germany

### EMPLOYMENT

June 1902 –	Technical Expert, III Class <i>Federal Office for Intellectual Property,</i> Bern, Switzerland
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## PUBLICATIONS

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Articles in peer-reviewed journals:

1. Einstein, A. Über die von der molekularkinetischen Theorie der Wärme geforderte Bewegung von in ruhenden Flüssigkeiten suspendierten Teilchen. *Annalen der Physik* **322**, 549 (1905).
2. Einstein, A. Zur Elektrodynamik bewegter Körper. *Annalen der Physik* **322**, 891 (1905).

Conference contributions:

3. Einstein, A. *Implications of a fixed vacuum speed of light in Relativity* Oct. 2–6, 1905 (1st Conference on Special Relativity, Zurich, Switzerland).