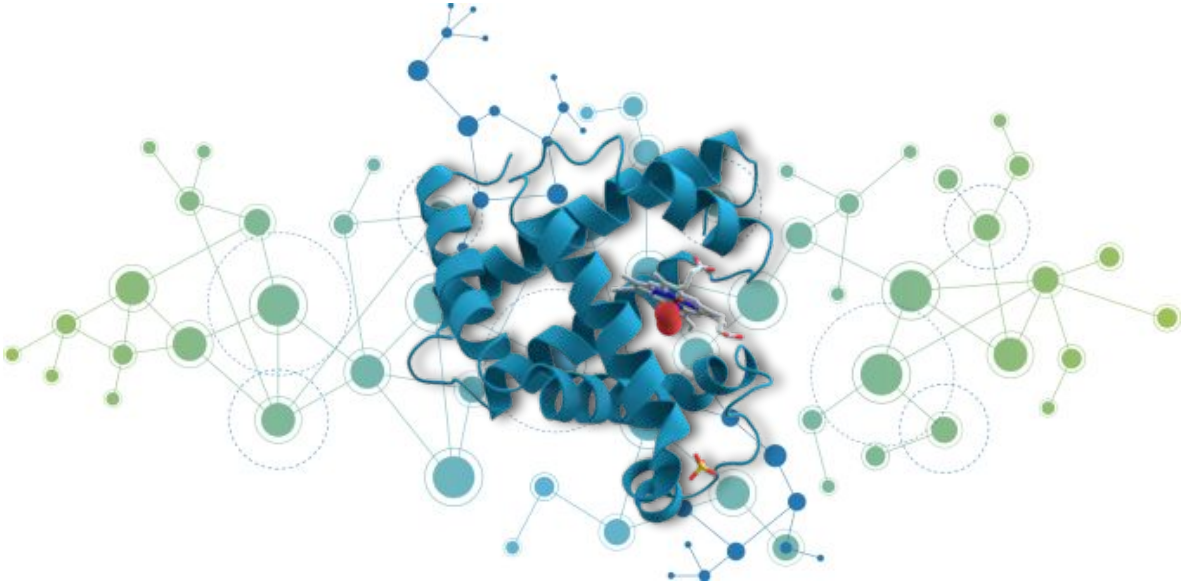
A Brief Talk on the Importance of

Natural Language Processing in Biomedicine



Simone Conia

Reading Group @ Sapienza NLP

September 16th, 2020

SAPIENZA
UNIVERSITÀ DI ROMA

Language models are taking NLP to the next level

NLP is witnessing an unprecedented growth thanks to the expressiveness and wide availability of (pretrained) language models such as ELMo [1], BERT [2] and GPT [3].

[1] Deep contextualized word representations, Peters et al., 2018
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[3] Improving Language Understanding by Generative Pre-Training, Radford et al., 2018

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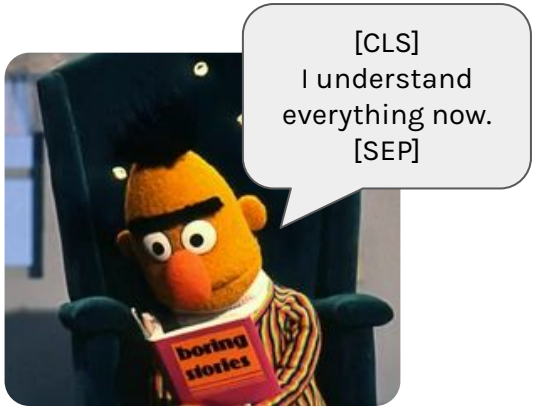
Language models encode information that has been proven to be fundamental in a wide array of "language understanding" tasks such as question answering and natural language inference.



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Language models are here to stay

Research on language models is not slowing down!

Larger!
G-Shard [4] with 1 trillion parameters.

[4] GShard: Scaling Giant Models with Conditional Computation and Automatic Sharding, Lepikhin et al., 2020
[5] Reformer: The Efficient Transformer, Kitaev et al., 2020
[6] Exploring the Limits of Transfer Learning with a Unified Text-to-Text Transformer, Raffel et al., 2019
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Knowledge!
REALM [7] exploits Wikipedia articles.

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NLP + Biomedicine

How can language models help research and researchers in Biomedicine?

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Automatically find names of people, places, and organizations in text across many languages.

Text Mining
for biomedical documents

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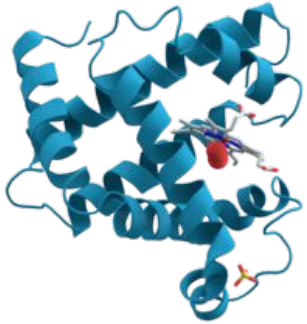

Research
on molecules, diseases and drugs

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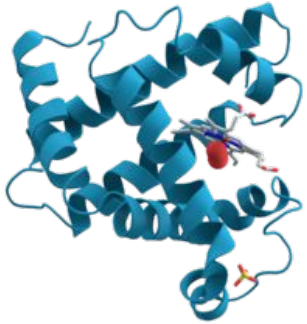

Research
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from traditional to innovative applications!

Preliminaries: a step back to language modeling

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Therefore a language model must "understand" sentences.* Notice that syntax alone is often not enough.

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Idea: do not build a new system for each task, **adapt an existing language model!**

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For this talk, we only need to know that BERT is a recently proposed (masked) language model that learns to guess missing words on a huge amount of text.

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Correctly guessing words requires BERT to "**smurf**" from the context of a sentence.

As a consequence, BERT learns good word representations that can be **smurfed** in other tasks.

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That's all we need to know for now about BERT!

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Text Analysis and Mining in Biomedicine

Text Analysis/Mining is the process of extracting meaningful/relevant information from unstructured text data (e.g. books, websites, reviews, articles, etc.).

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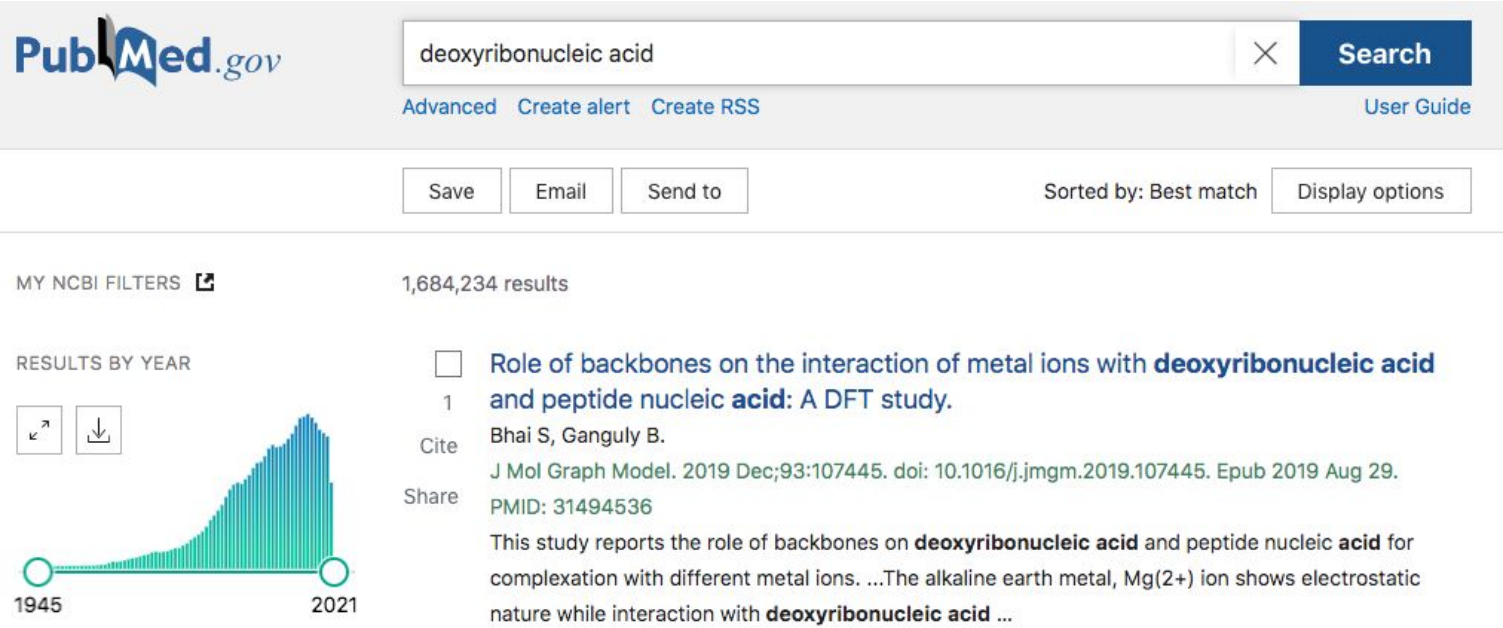

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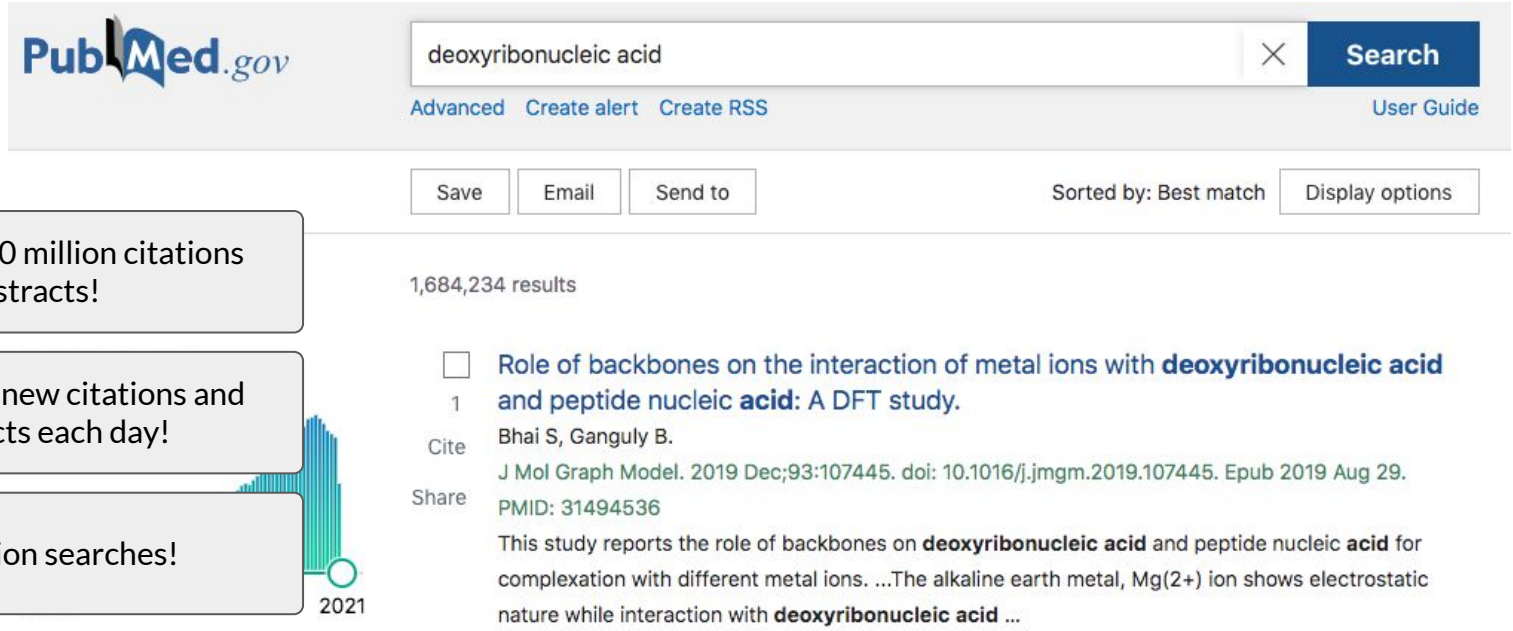

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3000+ new citations and abstracts each day!

3.3 billion searches!

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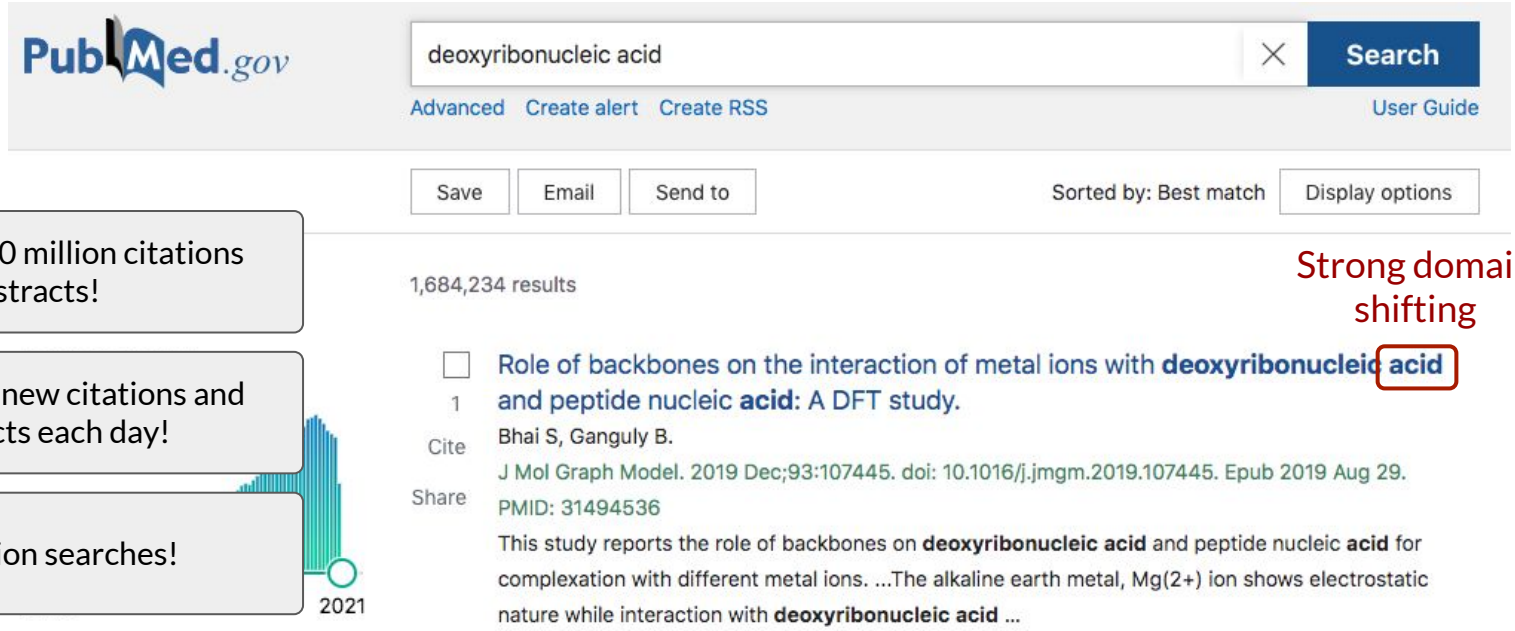

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Strong domain shifting

BioBERT: specializing BERT for biomedical text mining

BERT is extremely easy to specialize as long as domain-specific text data is available in large quantities.

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BERT
pretrained on Wikipedia
and BookCorpus

PubMed
abstracts and full
text articles

BioBERT

[8] BioBERT: a pre-trained biomedical language representation model for biomedical text mining, Lee et al., 2019

BioBERT: zero supervision, no feature engineering

BioBERT is a leap forward in biomedical text mining!

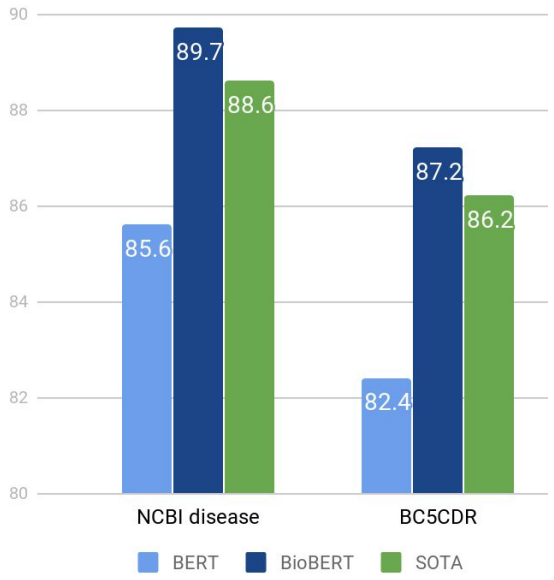
BioBERT

Compared to previous approaches:

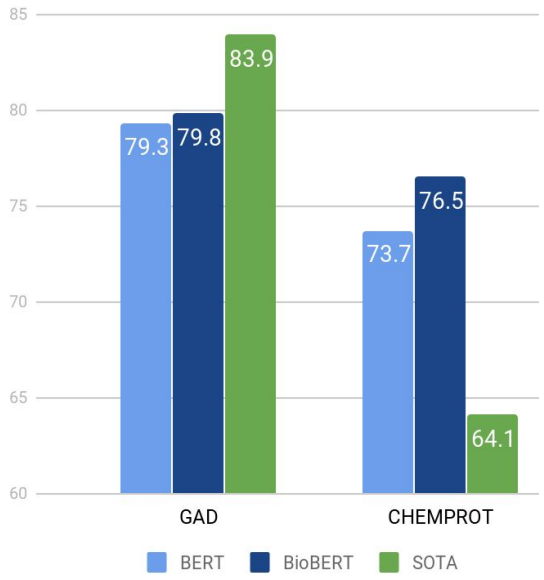
- No complex **preprocessing** strategies
- No need for specialized **task-specific architectures**
- No need for large amounts of **labeled** data
- No **biomedical expertise** required

BioBERT: evaluation on biomedical tasks

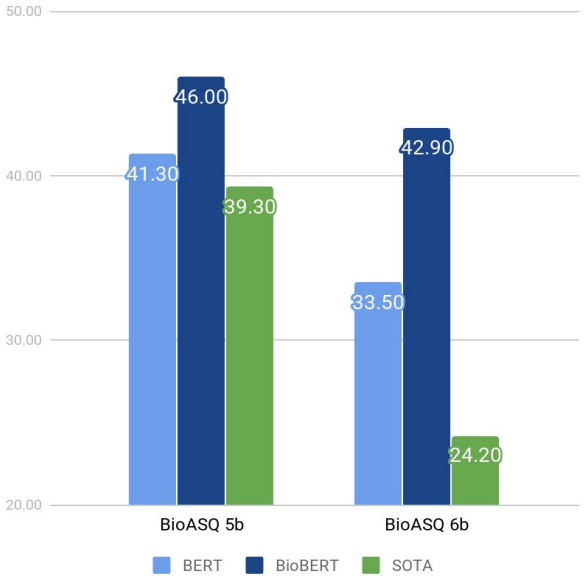
Named Entity Recognition
(F1 Score)



Relation Extraction
(F1 Score)

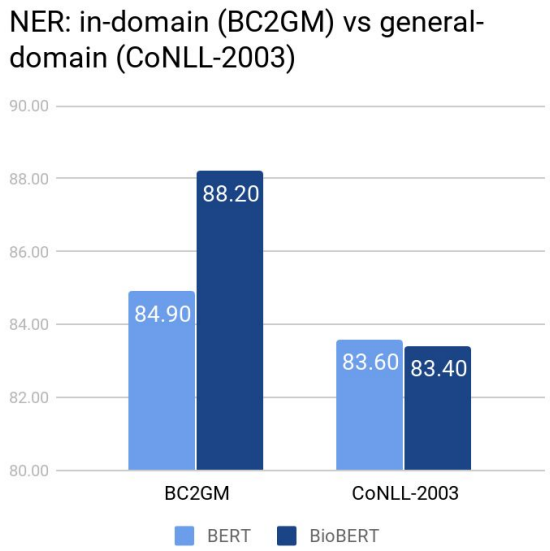


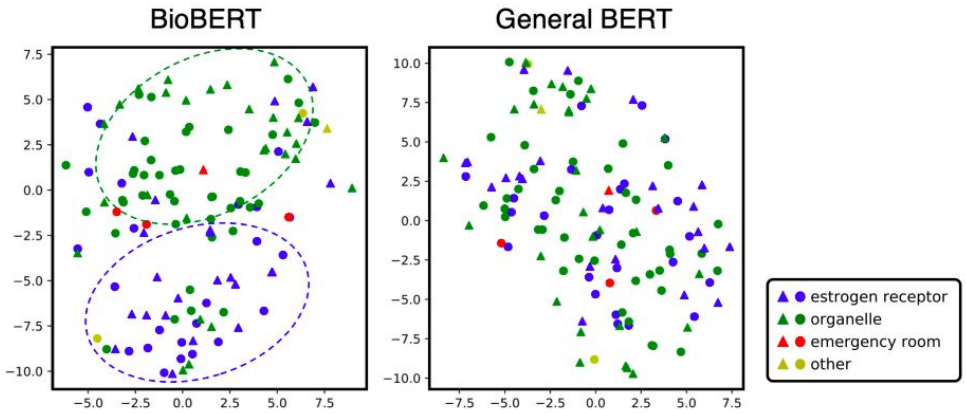
Question Answering
(Accuracy)



BioBERT: in-domain and general-domain generalization

Jin et al. (2019) show that the drop in performance of BioBERT on general-domain data (CoNLL-2003) is negligible.





[9] Probing Biomedical Embeddings from Language Models, Jin et al., 2019

Growing interest in biomedicine: MEDIQA 2019 @ ACL

The growing interest in NLP applied to medicine is also proved by the organization of several workshops and shared tasks.

MEDIQA [10] proposed 3 shared tasks:

1. Natural Language Inference
2. Question Entailment Recognition
3. Question Answering

72 participants!

[10] Overview of the MEDIQA 2019 Shared Task on Textual Inference, Question Entailment and Question Answering, Abacha et al., 2019

Growing interest in biomedicine: W-NUT 2020 @ EMNLP

The growing interest in NLP applied to medicine is also proved by the organization of several workshops and shared tasks.

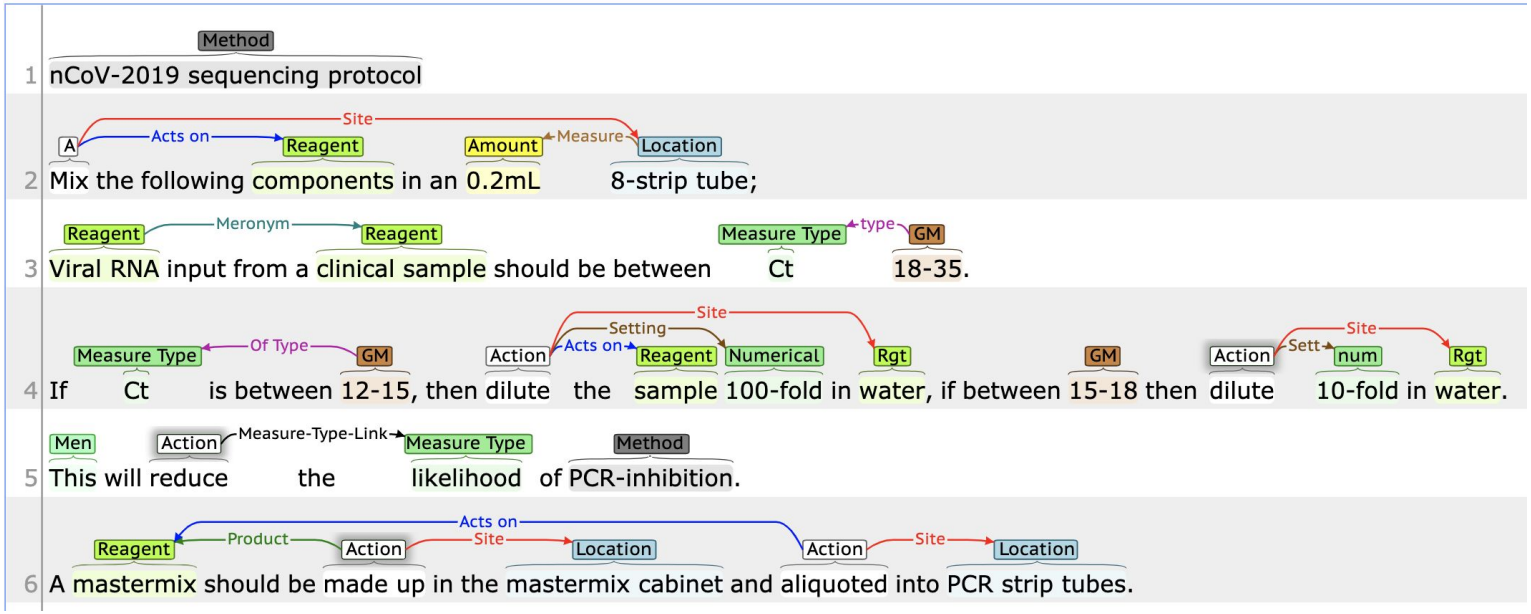
W-NUT [11] is proposing 3 shared tasks:

1. **Entity and Relation Recognition over wet-lab protocols**
2. Identification of Informative COVID-19 English Tweets
3. COVID-19 Event Extraction from Twitter

[11] http://noisy-text.github.io/2020/

Entity and Relation Recognition over wet-lab protocols

Lab protocols specify steps in performing a lab procedure. They are noisy, dense, and domain-specific. System entries are invited for event recognition and relation extraction over these lab protocols.



ClinicalBERT: specializing BERT on clinical notes

BERT is also finding application in healthcare thanks to its flexibility.

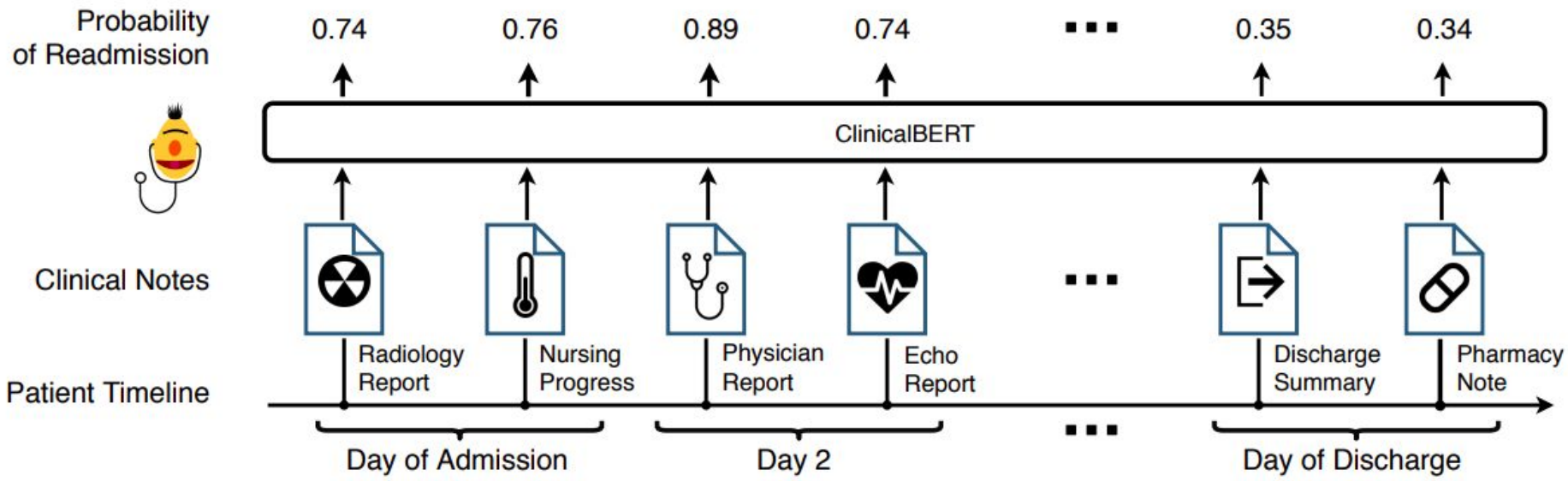
BERT
pretrained on Wikipedia
and BookCorpus

Clinical notes
about patient
medical histories

ClinicalBERT

[12] ClinicalBERT: Modeling Clinical Notes and Predicting Hospital Readmission, Huang et al., 2019

ClinicalBERT: predicting hospital readmissions



ClinicalBERT: avoiding wastes and improving patients' QoL

While the idea behind ClinicalBERT is relatively simple, it can have a great impact for **hospitals**:

- Readmissions cause an estimated annual (avoidable) cost of **17 billion dollars**.
- For each readmission, doctors and nurses must **reread dozens of clinical notes**.

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But also for **patients**:

- Readmissions may cause **traumas** or require **longer treatments**.
- Increased **healthcare-related expenses**.

New frontiers: self-supervised NLP for biomedical research

Many fundamental molecules in our bodies can be represented as sequences.

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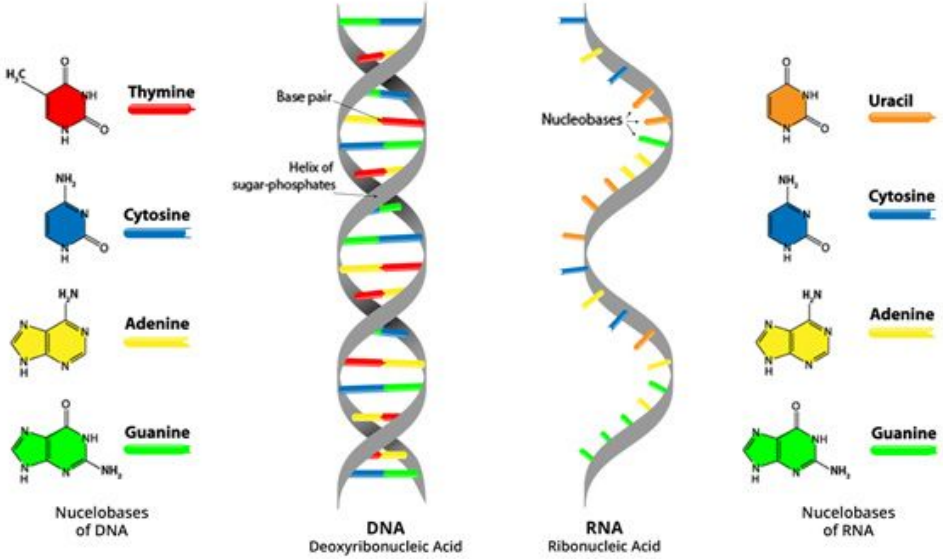
Can we apply NLP techniques to DNA modelling?



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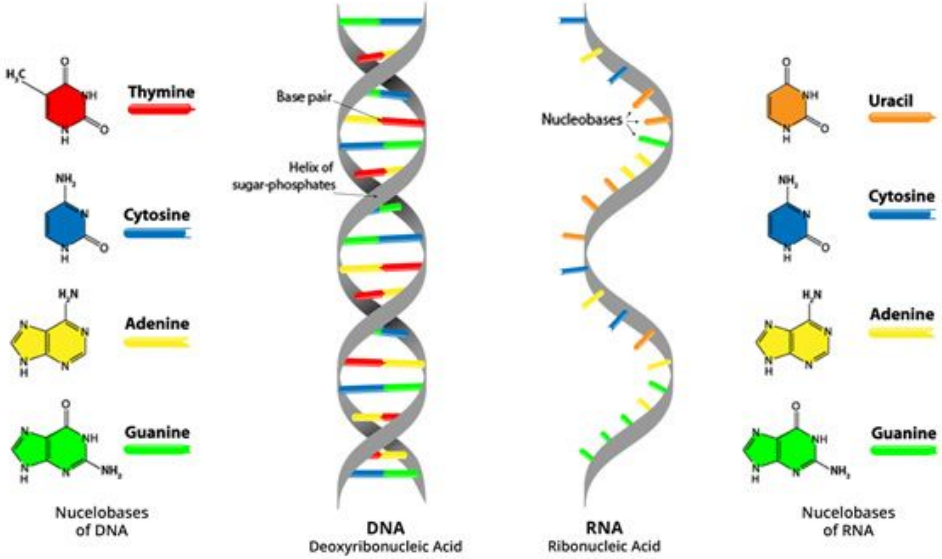
Yes!

- It's a sequence.
- Only 4 nucleosides.

But...



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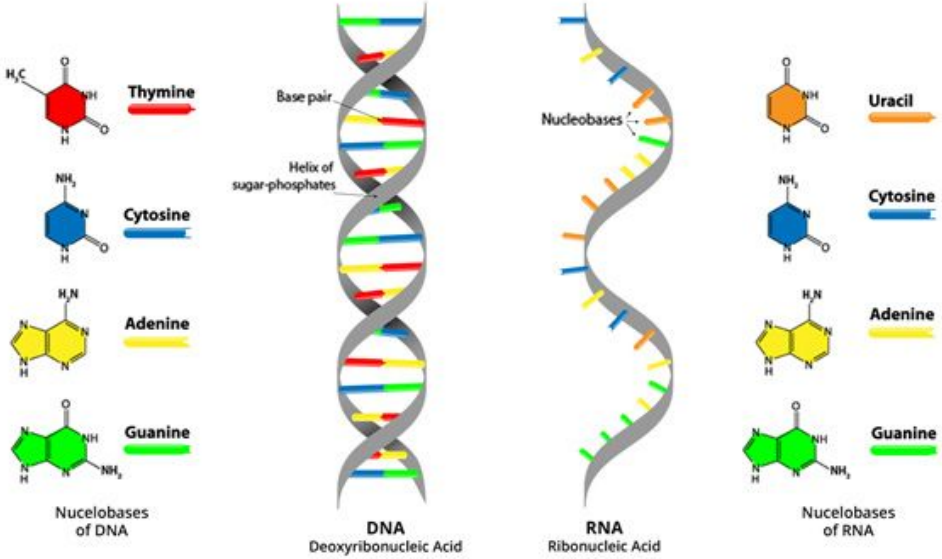


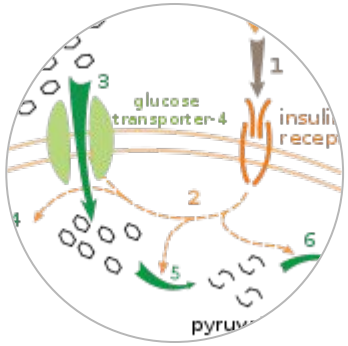
No...

- Too long sequences.

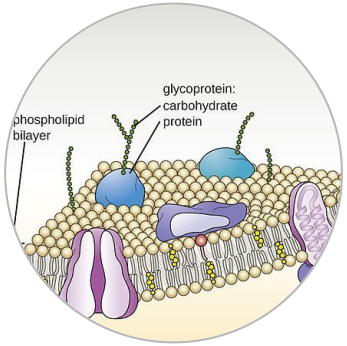
A human DNA molecule has up to 250 million nucleosides...

Proteins: a brief introduction

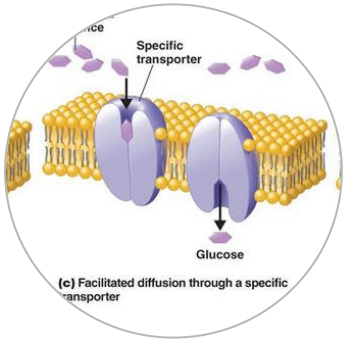
Proteins are biomolecules that play a fundamental role within our organisms.



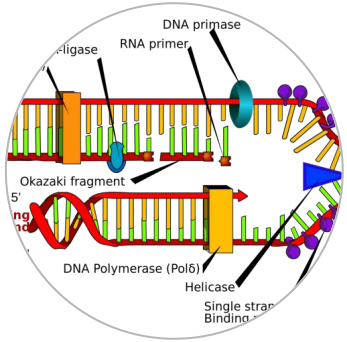
Metabolism
to convert food to energy.



Cell structure
is often provided by proteins.



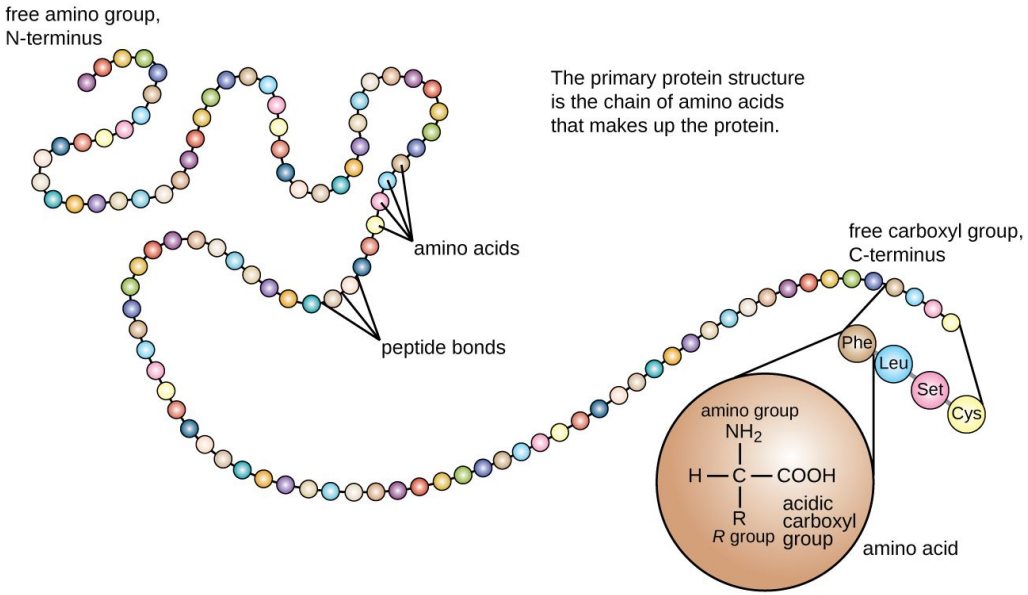
Transport
of other molecules.



Replication
of DNA and RNA molecules.

Proteins: sequences of amino acids

In their simplest form, proteins can be seen as sequences of smaller molecules called amino acids.



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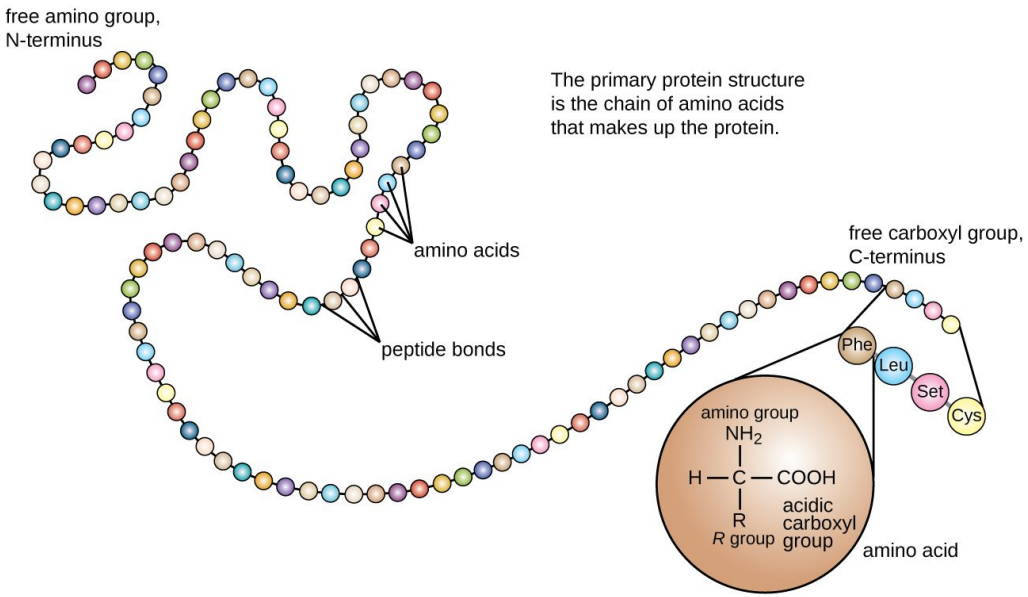

Good news:

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- A sequence is believed to completely characterize a protein's behavior.

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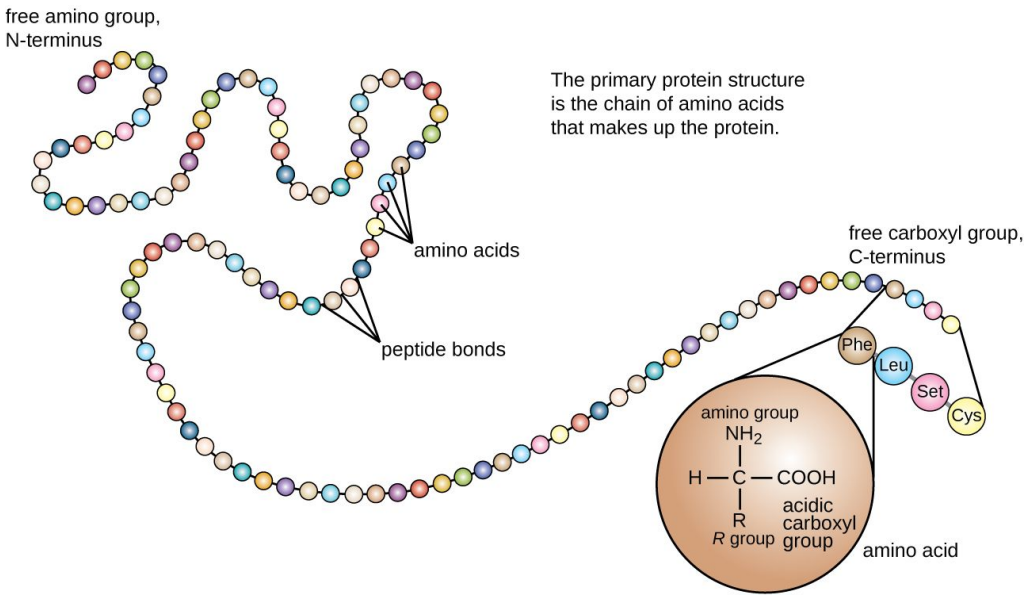

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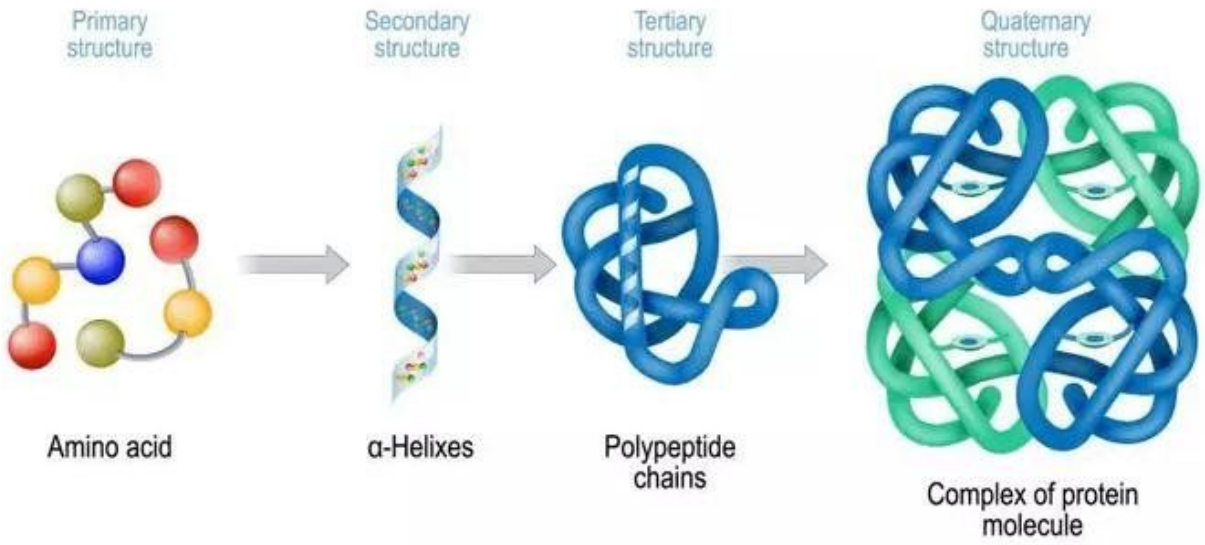
Bad news:

- Amino acid interactions are not linear, i.e., they may interact even if they are separated by hundreds of other amino acids.

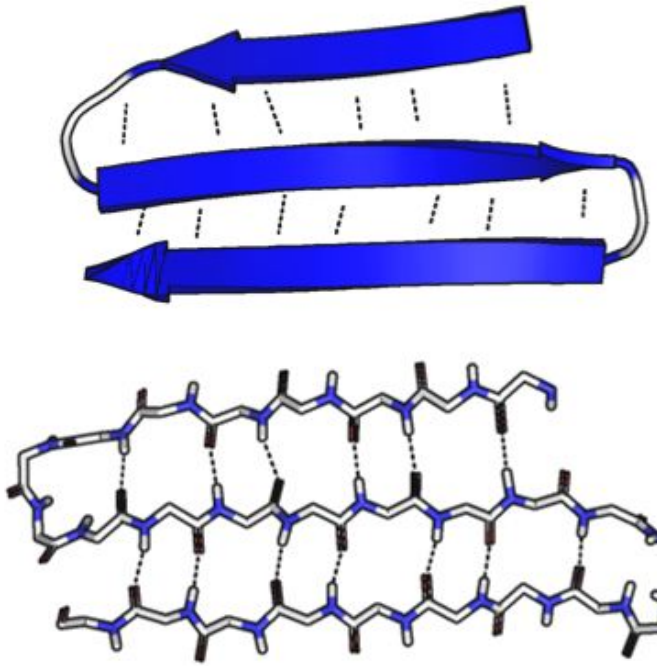
Proteins: structure



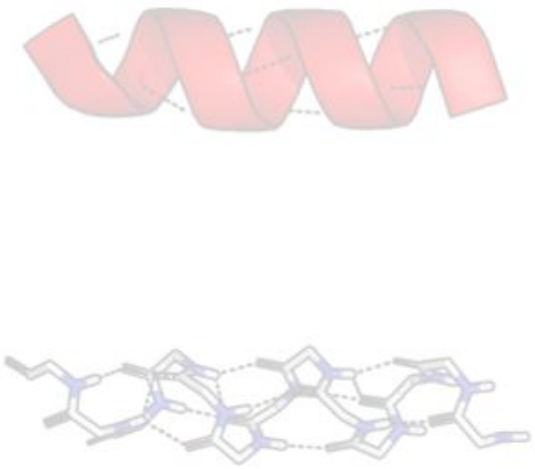
There is also a quinary structure...

Proteins: secondary structure

Secondary



β-Sheet (3 strands)



α-helix

Proteins: secondary structure

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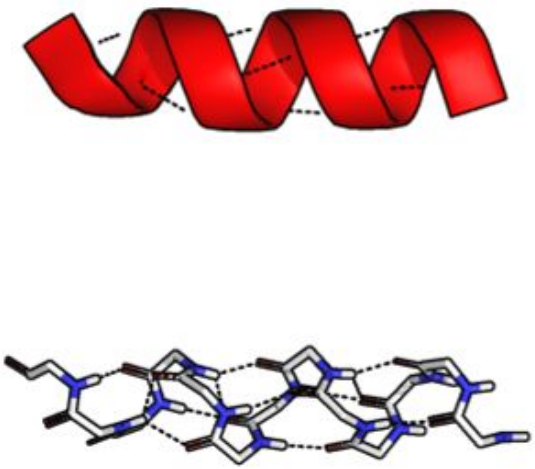
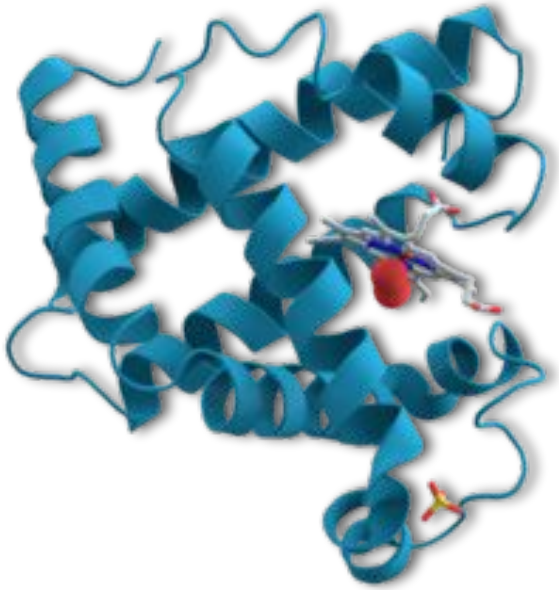


α-helix

Proteins: tertiary structure



Folding, Unfolding and Refolding

As of now, there is no general and accurate folding model, so researchers mostly still rely on experience, intuition and lengthy trials.

Evaluating Protein Transfer Learning with TAPE

Simple idea: train a language model (e.g. BERT) on a large amount of amino acids sequences.

```
MSKGEELFTG VVPILVELDG DVNGHKFSVS GEGEGDATYG KLTLKFICTT
GKLPVPWPTL VTTFSYGVQC FSRYPDHMKQ HDFFKSAMPE GYVQERTIFF
KDDGNYKTRA EVKFEGDTLV NRIELKGIDF KEDGNILGHK LEYNYNSHNV
YIMADKQKNG IKVNFKIRHN IEDGSVQLAD HYQQNTPIGD GPVLLPDNHY
LSTQSALSKD PNEKRDHMVL LEFVTAAGIT HGMDELYK
```

[13] Evaluating Protein Transfer Learning with TAPE, Rao et al., 2019

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```
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GKLPVPW[redacted]TL VTTFSYGVQC [redacted]YPDHMKQ HDFFK[redacted]AMP[redacted] GYVQERTIFF
KDD[redacted]NYKTRA EVK[redacted]EGDT[redacted]V N[redacted]IELKGIDF KEDGNILGHK L[redacted]YNYNSH[redacted]V
YIMADKQ[redacted]NG IKVNFKIRHN I[redacted]D[redacted]SVQLAD [redacted]YQQNTPIGD GPVL[redacted]PDNHY
LSTQSALSKD PN[redacted]DHMVL LEFVTAAGIT HGMDELYK
```

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Simple idea: train a language model (e.g. BERT) on a large amount of amino acids sequences.

Then, further train the pretrained language model on a complex protein task such as secondary and tertiary structure prediction, where labeled data may be scarce.

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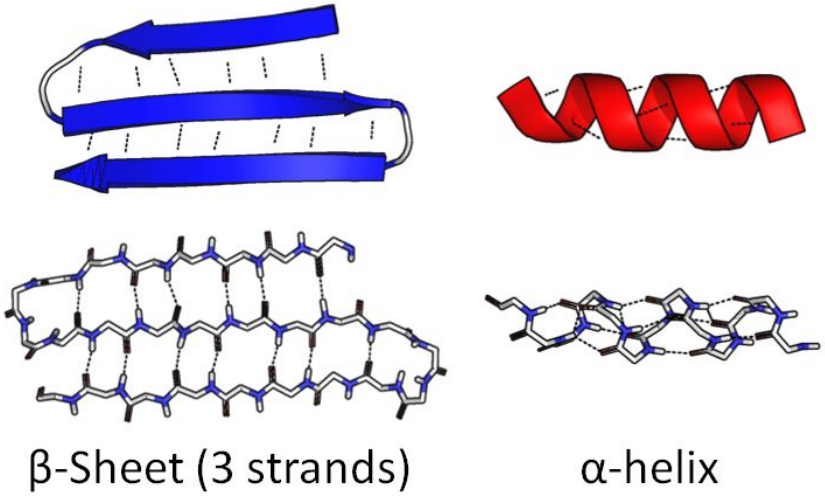
Datasets:

- **Protein Data Bank** (PDB): 160’000 protein sequences.
- **UniParc**: 300’000’000 protein sequences.

[13] Evaluating Protein Transfer Learning with TAPE, Rao et al., 2019

Secondary Structure Prediction

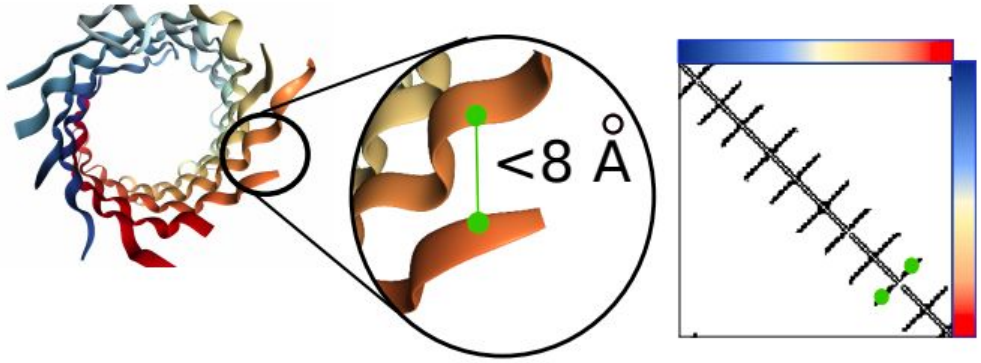
Determine whether an amino acid in the protein belongs to an alpha helix or beta sheet or neither of them.



Understanding local structure and amino acid interactions.

Contact Prediction

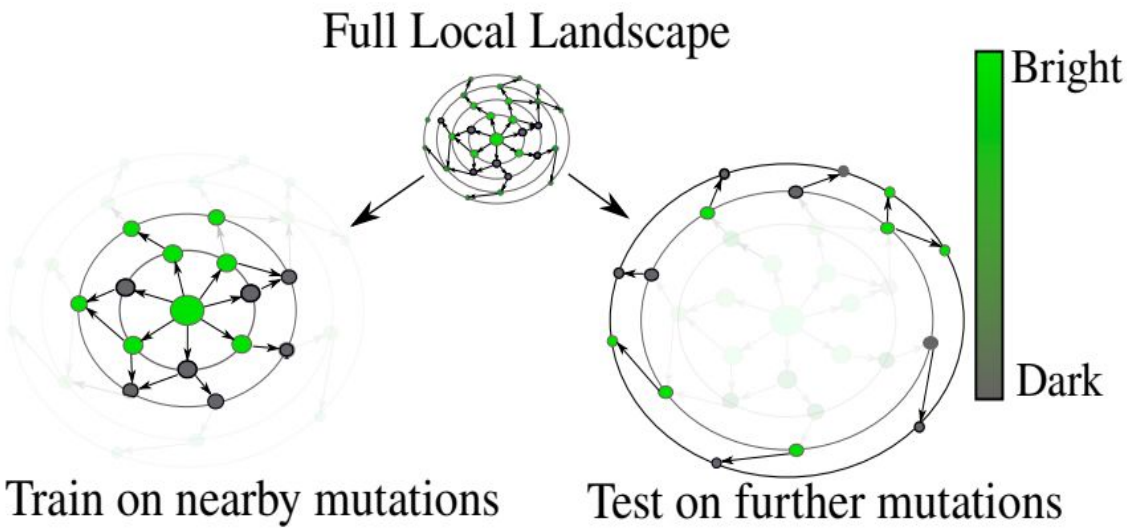
Related to tertiary structure prediction, consists in determining whether two non-consecutive amino acids are 3-dimensionally close in the folded protein.



Understanding global structure and amino acid interactions.

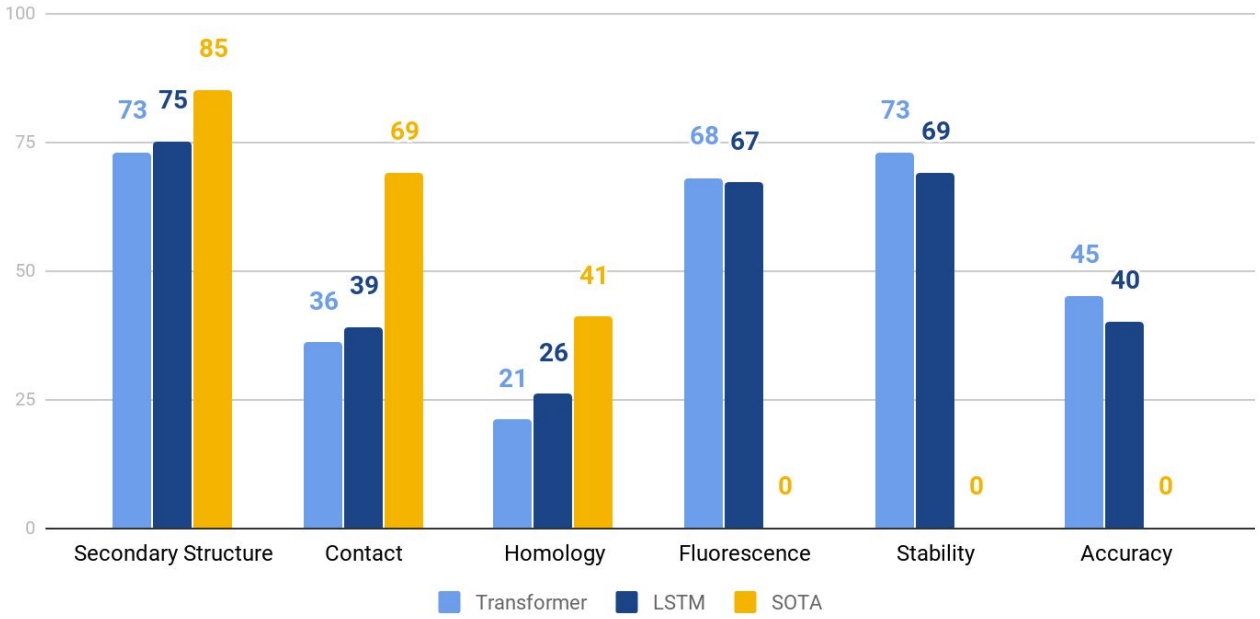
Fluorescence test: genotypes and phenotypes

Related to the overall behavior of a protein, consists in determining whether a mutation of a single amino acid changes the characteristics of the protein.



Results: self-supervision and pretraining work!

Simple self-supervision and language model pretraining show promising results, even though there is still a significant gap to bridge with respect to complex specialized models.



Learning the “language” of proteins

The NeurIPS work of Rao et al. (2019) showed that self-supervised language modeling is a promising direction for future protein models.

- Compared to specialized architectures, **one language model fits multiple tasks**.
- Rao et al. (2019) experiment with **a relatively small model**, “only” 38M parameters.
- **No feature engineering is required** for any of the proposed models.

Conclusion

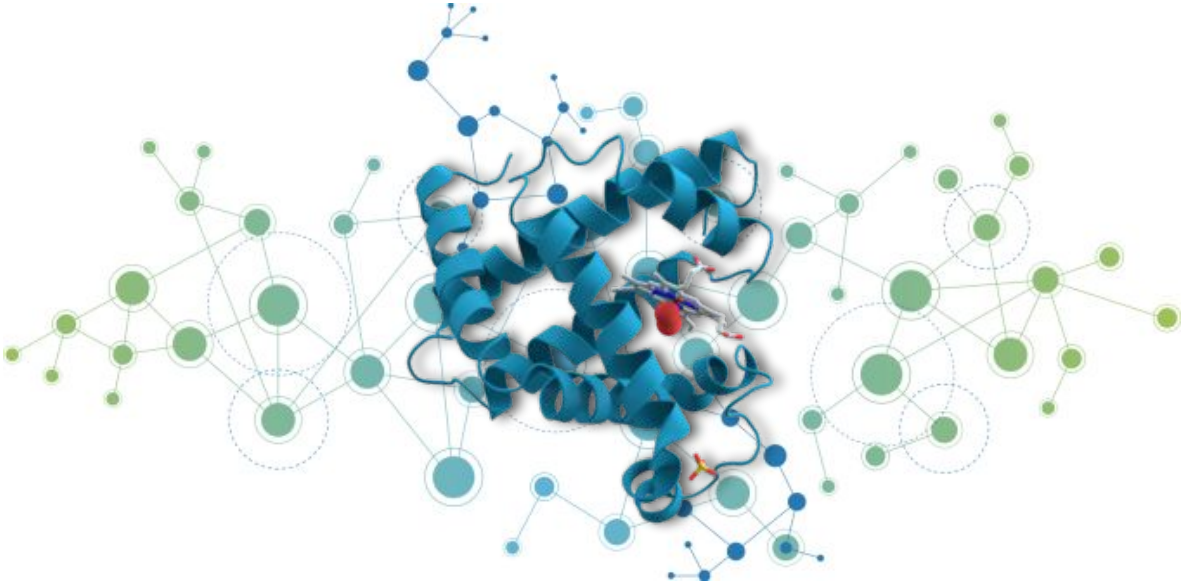
Today we have seen self-supervised language model pretraining for:

- Biomedical text analysis and text mining.
- Real-life clinical situations.
- Basic research on protein modeling.

The future for self-supervised pretraining techniques in language modeling looks brighter and brighter!

Feel free to ask questions,

Thanks for your attention!



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September 16th, 2020

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