BioMedical NLP

Class 1
NLP Master's Programme, University of Bucharest

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Organization

Materials:

slides, book, conference/workshop proceedings

Workshops:

- Biomedical Natural Language Processing Workshop (BioNLP)
- Special Interest Group on Biomedical Natural Language Processing
- Clinical NLP Workshop
- Workshop on Computational Linguistics and Clinical Psychology
- Scholarly Document Processing Workshop

Organization

Topics we will discuss:

8. CONŢINUTURI
CONTENT

8.1. Curs Course
Introduction, main problems, relationship with other disciplines / Introducere in domeniu, probleme, relatii cu alte discipline
Resources and frameworks for bio-medical NLP / Resurse si unelte pentru NLP în domeniul medical
Medical information retrieval and information extraction / Regasirea informatiei si extragerea informatiei din date medicale
Processing Electronic Health Records (EHRs) / Procesarea dosarelor medicale electronice
Scientific document analysis: parsing, organizing and retrieving scientific information Analiza documentelor științifice: prelucrarea, organizarea și regăsirea informației științifice
Applications of NLP is psychology. Mental health problems - computational approaches / Aplicații ale procesării limbajului natural în psihologie. Abordari computationale pentru analiza problemelor mentale
Depression. NLP & multimodal based approaches / Abordari computationale ale depresiei cu tehnici de procesare a limbajului natural și multimodale
Physical and mental health in social media: information and misinformation / Sanatatea si social media: informatie si dezinformare
Ethical issues and privacy protection in processing medical data, ethics & fairness in AI models / Probleme de etica si confidentialitate in procesarea datelor medicale, etică și echitabilitate în folosirea IA
NLP-specific model architectures for other types of biomedical data Utilizarea modelelor specifice NLP pentru prelucrarea altor tipuri de date biomedicale
Recent research topics (main conferences and workshops ACL, EMNLP, NAACL; BioNLP, CLPsych etc.) / Teme recente de cercetare in domeniu (articole recente din principalele forumuri si workshopuri asociate - ACL, EMNLP, NAACL; BioNLP, CLPsych etc)

2/5

Organization

Topics we will discuss:

https://drive.google.com/file/d/19-UPFBEWtHD8WuCq0WpiVbm4pz29wLbD/view?usp=share_link

BioMedical NLP

Universal end goal for using technology in biomedicine: All in all, general end goal: **improving quality of life through understanding life processes.**

Useful for: doctors, patients, other actors in the medical system (insurance, policy makers); researchers, maintainers of resources used in biology/medicine research

BioMedical NLP

BioMedical NLP = part of the wider area of Artificial Intelligence for Medicine / bio-informatics

BioMedical NLP = the use of **NLP methods** for helping biology and medicine research, clinical practice, and adjacent areas

Relations to other disciplines

- medicine...
- psychology
- genetics/genomics
- biology
- other NLP subdomains: information retrieval, NER, knowledge representation
- other types of AI/ML in medicine:
  - computer vision
  - robotics
  - .....

Relations to other disciplines

Why general NLP is not enough

- most NLP has focused on different types of data (generic, public, ...)
- we do have large volumes of data in biological and medical domain
  - problems around privacy and organizing data
  - problems with annotating data - requires expertise
- general sense representations don't do a good job for medical terms; specific meanings, important distinctions

Relations to other disciplines

Why general NLP is not enough

Semantic class	Examples
Cell lines	*T98G, HeLa cell, Chinese hamster ovary cells, CHO cells*
Cell types	*primary T lymphocytes, natural killer cells, NK cells*
Chemicals	*citric acid, 1,2-diiodopentane, C*
Drugs	*cyclosporin A, CDDP*
Genes/proteins	*white, HSP60, protein kinase C, L23A*
Malignancies	*carcinoma, breast neoplasms*
Medical/clinical concepts	*amyotrophic lateral sclerosis*
Mouse strains	*LAFT, AKR*
Mutations	*C10T, Ala64 → Gly*
Populations	*judo group*

Figure 22.31 A sample of the semantic classes of named entities that have been recognized in biomedical NLP. Note the surface similarities between many of the examples.

From *Speech and Language Processing: An Introduction to Speech Recognition, Computational Linguistics and Natural Language Processing: Second Edition, Daniel Jurafsky & James H. Martin. C*

Relations to other disciplines

Why general NLP is not enough

Biomedical Term	Category	BERT	SciBERT	PubMedBERT (Ours)
diabetes	disease	✓	✓	✓
leukemia	disease	✓	✓	✓
lithium	drug	✓	✓	✓
insulin	drug	✓	✓	✓
DNA	gene	✓	✓	✓
promoter	gene	✓	✓	✓
hypertension	disease		✓	✓
nephropathy	disease		✓	✓
lymphoma	disease		✓	✓
lidocaine	drug		✓	✓
oropharyngeal	organ			✓
cardiomyocyte	cell			✓
chloramphenicol	drug			✓
RecA	gene			✓
acetyltransferase	gene			✓
clonidine	drug			✓
naloxone	drug			✓

From Biomedical NLP Group - Microsoft Research

Relations to other disciplines

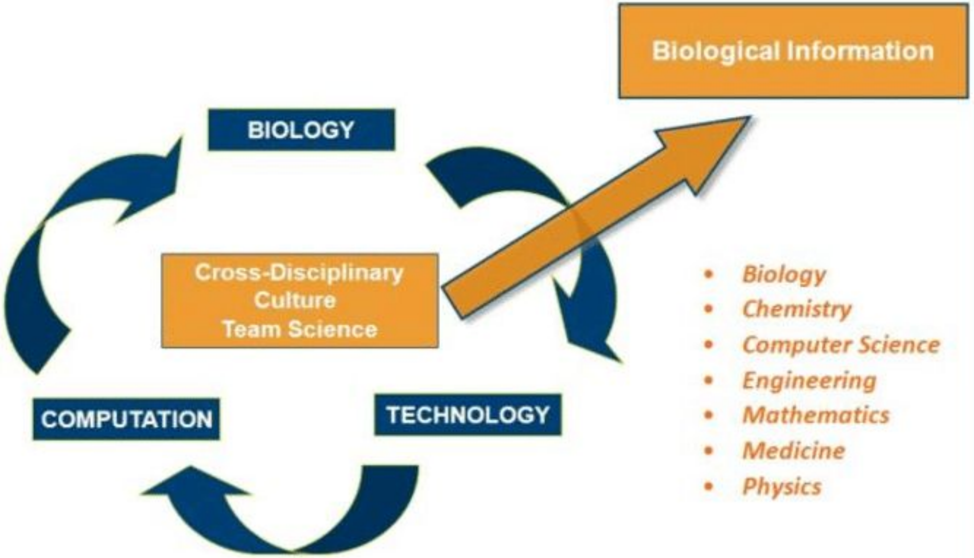
Applications in: "Everything from automated screening and diagnosis, adaptive clinical trials, operations research, global health, precision medicine, home health and wearables, genomic analysis, drug discovery and design, robotics, and many more."

Interdisciplinary - Healthcare ecosystem:

> "This includes AI developers, tech companies, policymakers and regulators, healthcare system leadership, pharmaceutical and device industry, frontline conditions, ethicists, even patients and patient caregivers.

Today in NLP still relatively niche community (smaller than the MT subdomain for example), not all include mental health (but we will); a few workshops: …

Relations to other disciplines



Holy trinity of the biological crossdisciplinary culture-"biology drives technology drives analytical tools revolutionizes biology." Biological breakthroughs require technological innovations which in turn necessitate new computing tools. New technological and computing tools, in turn, allow for the exploration of new biological frontiers.
(Systems Biology and P4 Medicine: Past, Present, and Future)

Importance of BioMedical NLP

Why is it important?...

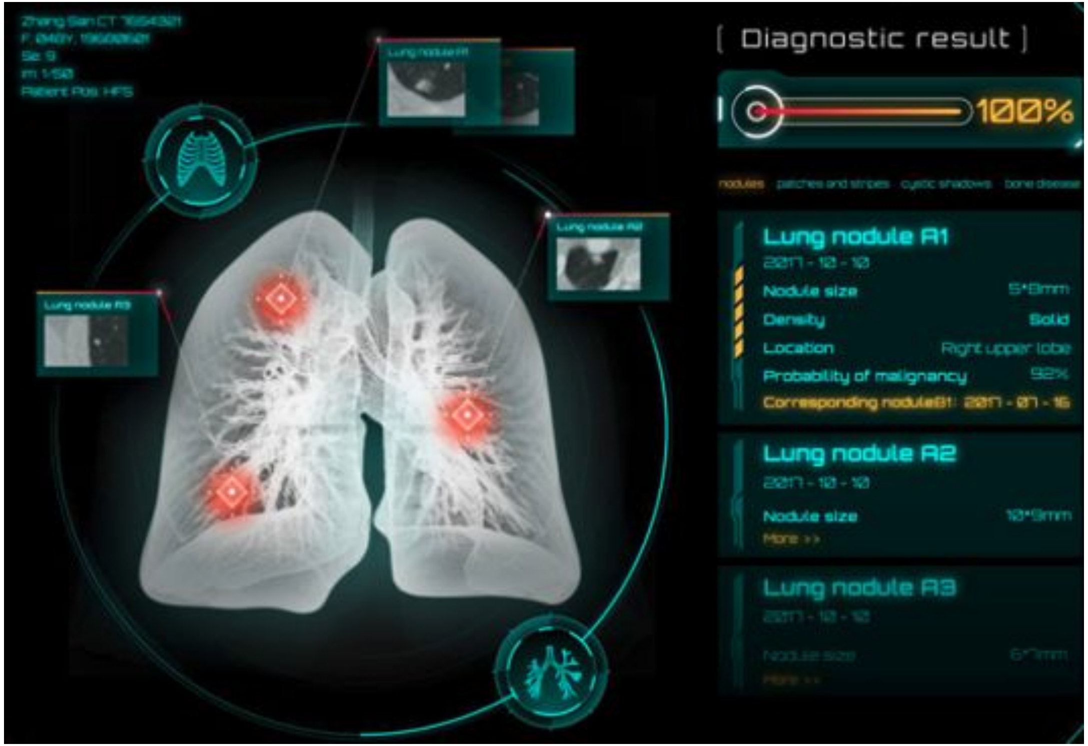
- helping with medical decisions in rare cases (diagnosis, predicting side effects, effectiveness...) based on medical records databases
- advancing research through retrieving information in existing research
- health assistant, insights (health data collected from various sources, smartwatches, social media activity etc)

Importance

Some examples of AI for healthcare:

- someone has a rare side effect in some treatment, doctors look into other patient’s medical records to make a decision
- detecting skin cancer with AI
- classifying tumors in radiology images
- the relevance of some genes for some diseases (discovered through analyzing occurrence in large amounts of research articles) leads to producing new targeted drugs

Importance


[Diagnostic result]
100%
Lung nodule A1
2017 - 10 - 10
Nodule size 5*8mm
Density Solid
Location Right upper lobe
Probability of malignancy 92%
Corresponding noduleB1: 2017 - 07 - 16
Lung nodule A2
2017 - 10 - 10
Nodule size 10*9mm
More >>
Lung nodule A3
2017 - 10 - 10

Importance

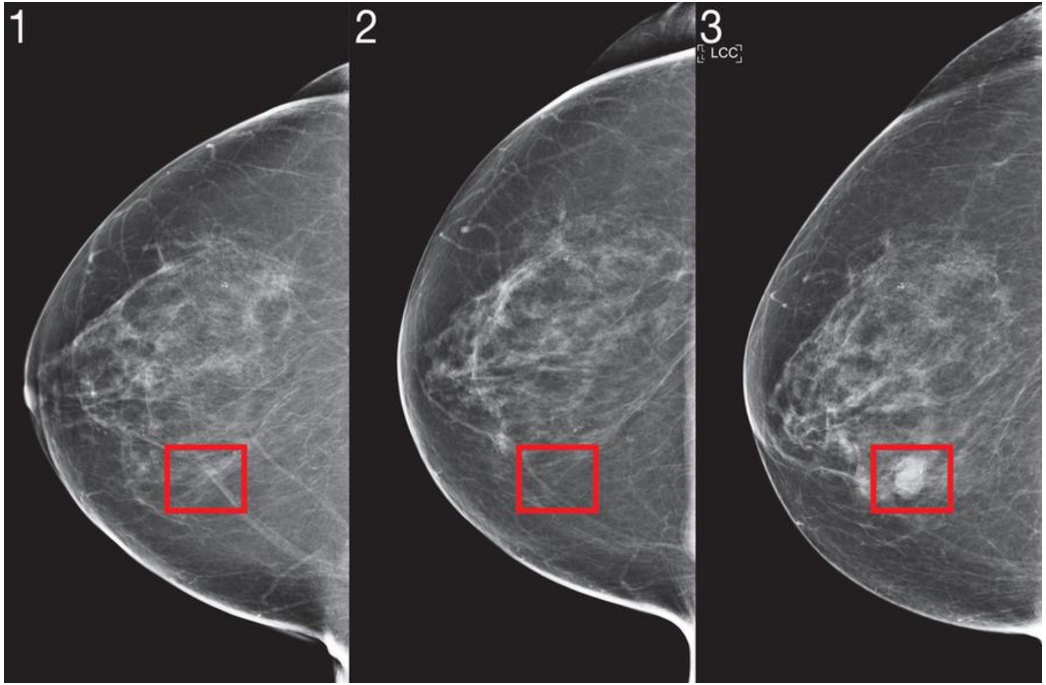
AI 'outperforms' doctors diagnosing breast cancer

Fergus Walsh
Medical correspondent
@BBCFergusWalsh

2 January 2020

https://www.bbc.com/news/health-50857759

Importance



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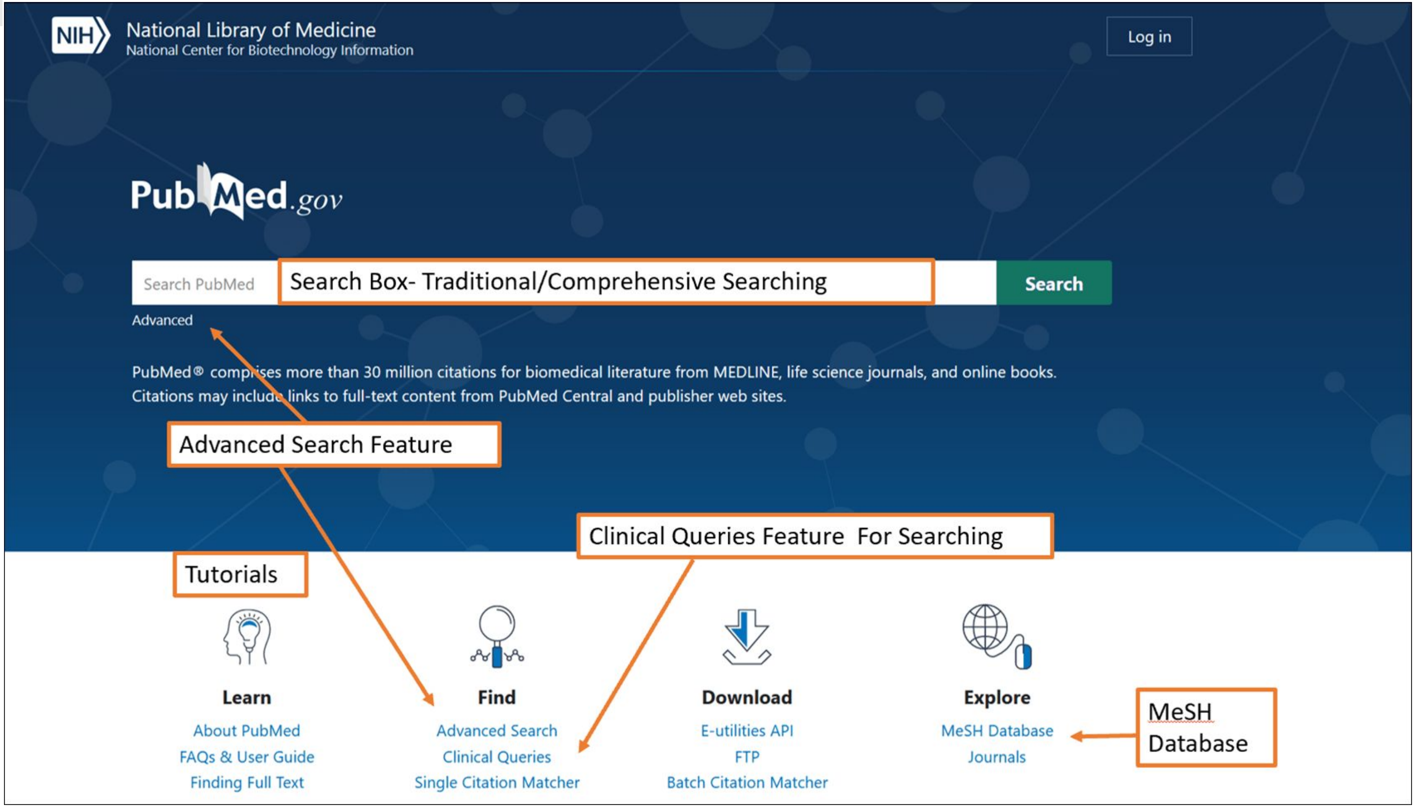
National Library of Medicine
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Search
Advanced
PubMed® comprises more than 30 million citations for biomedical literature from MEDLINE, life science journals, and online books. Citations may include links to full-text content from PubMed Central and publisher web sites.
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Clinical Queries Feature For Searching
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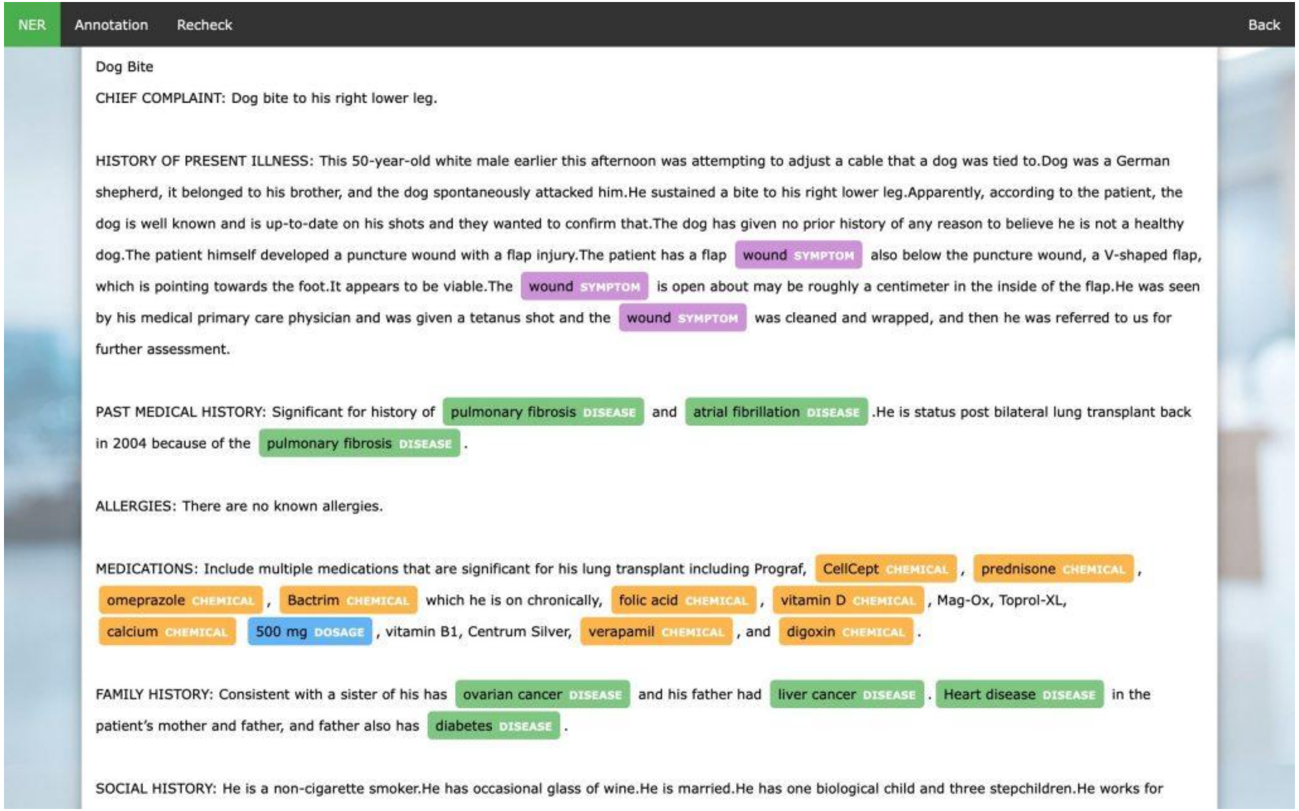
Explore
MeSH Database
Journals
MeSH Database

Importance



NER Annotation Recheck Back

Dog Bite

CHIEF COMPLAINT: Dog bite to his right lower leg.

HISTORY OF PRESENT ILLNESS: This 50-year-old white male earlier this afternoon was attempting to adjust a cable that a dog was tied to.Dog was a German shepherd, it belonged to his brother, and the dog spontaneously attacked him.He sustained a bite to his right lower leg.Apparently, according to the patient, the dog is well known and is up-to-date on his shots and they wanted to confirm that.The dog has given no prior history of any reason to believe he is not a healthy dog.The patient himself developed a puncture wound with a flap injury.The patient has a flap wound SYMPTOM also below the puncture wound, a V-shaped flap, which is pointing towards the foot.It appears to be viable.The wound SYMPTOM is open about may be roughly a centimeter in the inside of the flap.He was seen by his medical primary care physician and was given a tetanus shot and the wound SYMPTOM was cleaned and wrapped, and then he was referred to us for further assessment.

PAST MEDICAL HISTORY: Significant for history of pulmonary fibrosis DISEASE and atrial fibrillation DISEASE .He is status post bilateral lung transplant back in 2004 because of the pulmonary fibrosis DISEASE .

ALLERGIES: There are no known allergies.

MEDICATIONS: Include multiple medications that are significant for his lung transplant including Prograf, CellCept CHEMICAL , prednisone CHEMICAL , omeprazole CHEMICAL , Bactrim CHEMICAL which he is on chronically, folic acid CHEMICAL , vitamin D CHEMICAL , Mag-Ox, Toprol-XL, calcium CHEMICAL 500 mg DOSAGE , vitamin B1, Centrum Silver, verapamil CHEMICAL , and digoxin CHEMICAL .

FAMILY HISTORY: Consistent with a sister of his has ovarian cancer DISEASE and his father had liver cancer DISEASE . Heart disease DISEASE in the patient's mother and father, and father also has diabetes DISEASE .

SOCIAL HISTORY: He is a non-cigarette smoker.He has occasional glass of wine.He is married.He has one biological child and three stepchildren.He works for

Importance
Innovations in Healthcare: the Role of Technology

½ of deaths preventable in Romania (⅓ in EU)

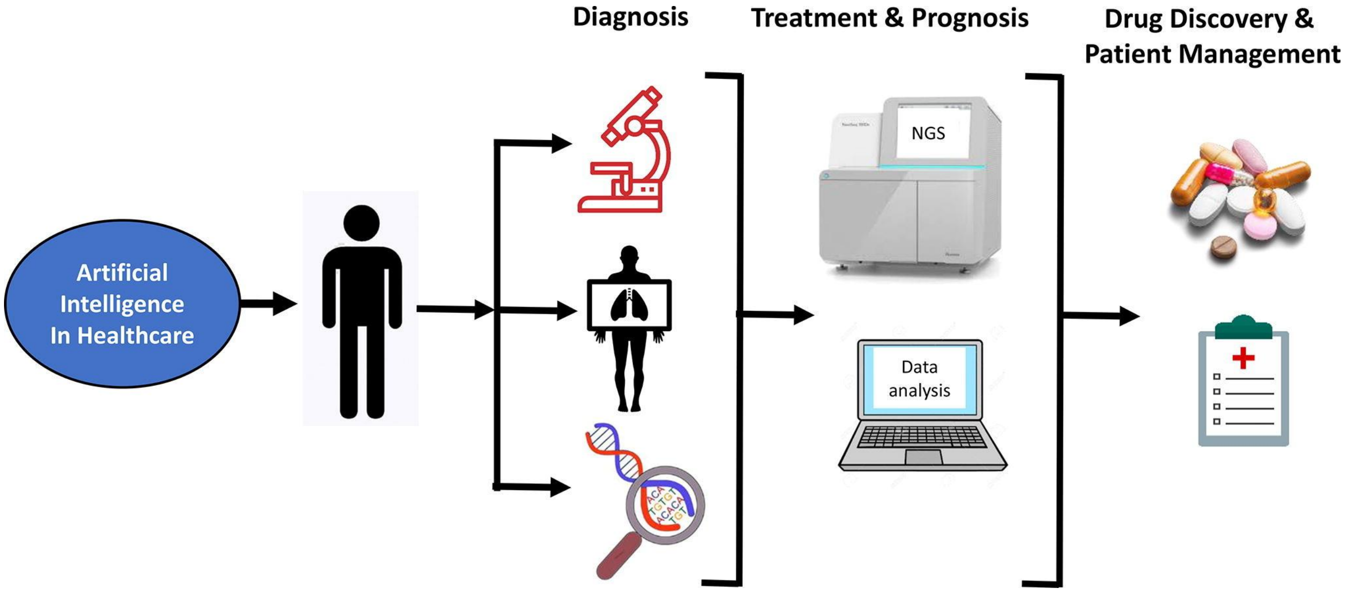
Large percentage of ineffective drugs across different diseases (“one size does not fit all”)

Recent **paradigm shift** in healthcare: the age of **personalized medicine** - individual phenotypes & genotypes to determine predisposition to disease (P4 medicine, “Virtual Patient Model”, computer-aided drug discovery)

Example innovation: targeted treatments for cancer based on genetic profile, increase effectiveness of treatment and life expectancy (e.g. small cell lung cancer)

Problem: the increase in data required for medical decisions > human cognitive capacity => technology to the rescue

Importance


Diagnosis
Treatment & Prognosis
Drug Discovery &
Patient Management
Artificial
Intelligence
In Healthcare
NGS
Data
analysis

Importance

Importance

TeleHealth
11010100
01010101
01101010
Phenome
Na143 K
3.7 BP
110/70
HCT32 BUN
Social Media
11010100
01010101
01101010
Epigenome
11010100
01010101
01101010
Genome
GCGTAG
ATGCGTA
GGCATGC
Transcriptome
UUAGUG
AUGCGU
CUAGGC
Proteome
arg-his-pro-
gly-leu-ser-
thr-ala-trp-
tyr-val-
Transactional
11010100
01010101
01101010
Single Cell
11010100
01010101
01101010
iPS Cells
11010100
01010101
01101010

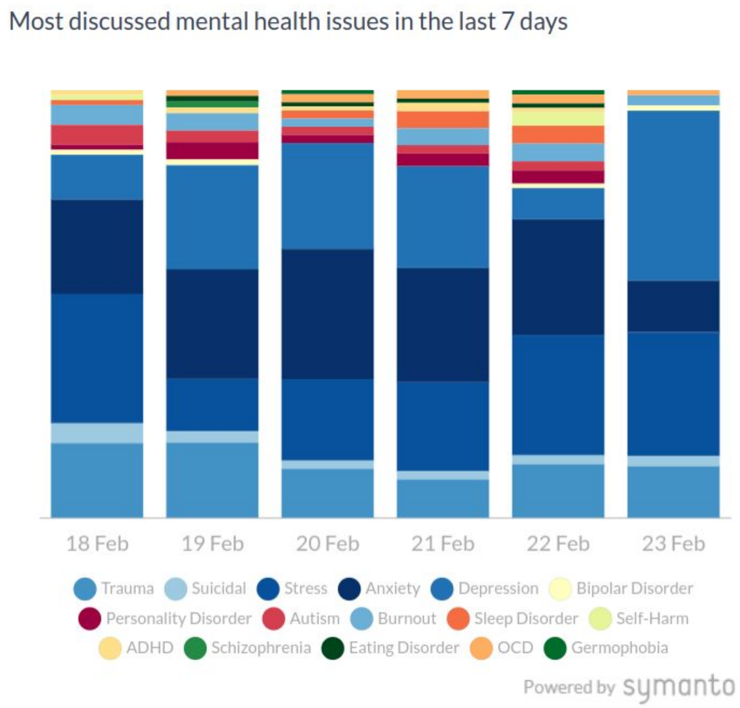
Importance

Example:

BioNTech a anunțat dezvoltarea unui nou instrument de monitorizarea a evoluției SARS-CoV2, Early Warning System, bazat pe inteligență artificială, care ar putea scurta timpul până la detectarea variantelor la risc înalt.

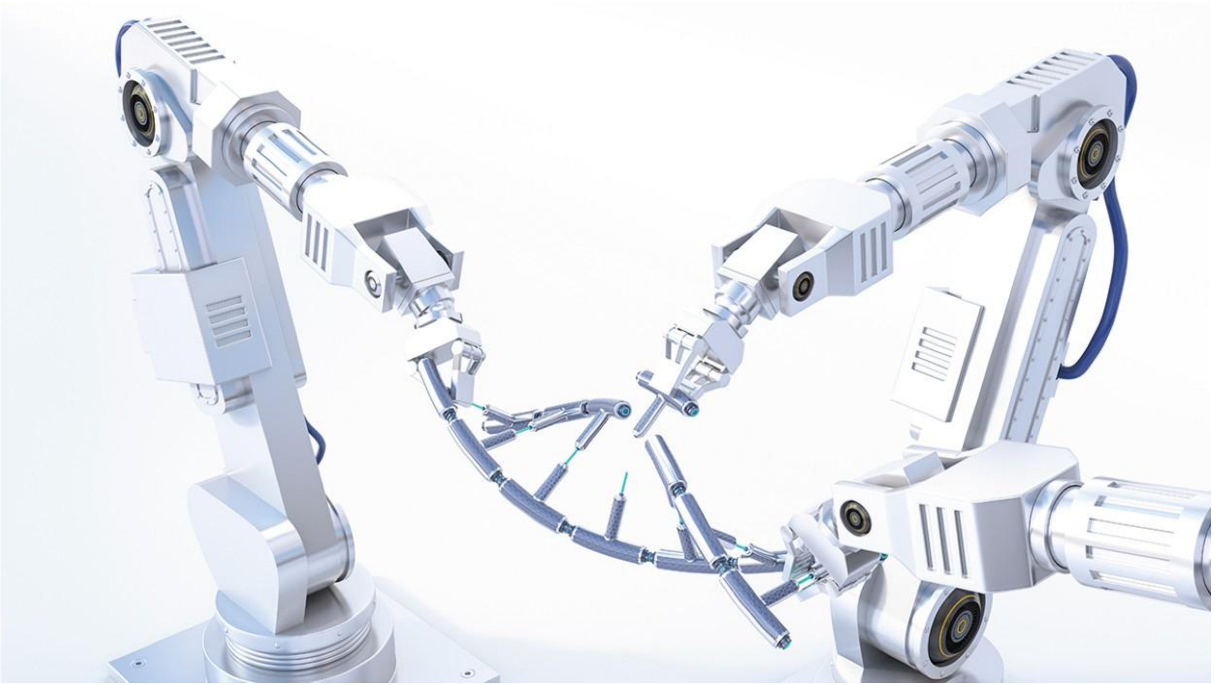
Prin modelarea datelor structurale legate de proteina spike și folosirea algoritmilor AI în cadrul platformei DeepChain, care prelucrează informațiile din bazele de date internaționale cu genomuri virale SARS-CoV-2, sistemul a permis detectarea cu două luni înainte a peste 90% din variantele raportate de OMS.

Importance



[Mental Health and Coronavirus | Live Impact Insights]

Importance



Importance

TABLE 1 | SELECTED RECENT FINANCINGS OF COMPANIES APPLYING AI IN DRUG DISCOVERY

Company	Date	Headline
Schrödinger	February 2020	Drug discovery software company closes $232 million IPO backed by Bill Gates and David Shaw.
Insitro	May 2020	Insitro raises $143 million in Series B funding, to help drive its machine learning-based drug discovery approaches further.
AbCellera	May 2020	AbCellera raises $105 million in Series B funding round to expand its antibody drug discovery platform.
Relay Therapeutics	July 2020	Relay Therapeutics, which focuses on understanding protein motion to design drug candidates, closes $400 million IPO.
Atomwise	August	Sanabil Investments co-leads $123 million Series B funding round for Atomwise to support the development of its molecule

[Tapping into the drug discovery potential of AI]

Types of data and users in bio-medical NLP

2 major areas:

- Mining clinical text <- improve healthcare outcomes
- Mining of biological publications <- advance knowledge of biology and medicine (discovery and understanding of fundamental physiological and pathological processes)

(borders disappearing in the case of personalized medical care based on fundamental biological studies)

3rd direction:

- User-generated data: social media etc; monitoring physical and mental health

Types of data and users in bio-medical NLP

Differences between subdomains and data types:

- types of text/data (heterogenous unstructured data in clinical domain vs papers in biological domain vs user-generated data);
- types and content of knowledge;
- available tools
    - scarcity of primary data in the case of the clinical domain vs papers in biological domain;
    - more lexical tools available for the clinical domain

Types of users

- clinicians: question-answering, document retrieval, ...
- coders: people assigning disease and procedure codes

Types of users

- model organisms database curators (model oraganisms e.g. mice, worm C elegans, zebra fish and genes in each): they are “crowd-produced”, they need curators to triage and organize source information; need tools like document triaging, NER tools
- biologists doing experimental work: since mid-1990s, technical advancements allowed them to work on thousands and 30,000 genes at a time (as opposed to one) => need text mining to gather statistics about their behavior from previously published literature : text mining, information extraction, paper summarization; leveraging text mining on papers to perform data analysis such as clustering genes

History of BioMedical NLP

History of BioMedical NLP - clinical

1960s:

1966: **ELIZA** - system capable of detecting medical terms in free text using pattern matching (Weizenbaum 1966) https://web.njit.edu/~ronkowit/eliza.html one of the first chatbots in NLP (chatbot therapist);

1969: APME (automatic processing of medical English) - generate semantic interpretation of input medical text with the goal of identifying diagnoses (Pratt et al). Was rule-based and made use of SNOP lexicon (Systematized Nomenclature of Pathology) - terms in different semantic categories, primitive grammar

History of BioMedical NLP - clinical

1970s:

first program for AI in medicine at Stanford (SUMEX-AIM) for clinical decision support

Resulted in:

- clinical applications, AI applications for diagnosis (infectious disease, diabetic retinopathy images), cancer drugs
- AI Handbook Project - materials to explain AI for healthcare audience (to improve their practice)

Initial ideas started to get real results along with other applications in AI, along with increase in data volume and computational power

History of BioMedical NLP - clinical

1980s:

identify biomedical concepts in patients' problem lists (e.g. SCAMP (Shapiro 1980));
Linguistic String Project - LSP: mapped facts extracted from clinical text into a structured database (Friedman et al 1983)

present:

more sophisticated systems being developed and used in clinical centers for extracting facts from clinical text, e.g. MedLEE (Medical Language Extraction and Encoding System),
using lexicon, grammar, formal sentence representation, used for:

- adverse event discovery,
- risks of developing breast cancer,
- association between diseases and drugs
- ...

History of BioMedical NLP - clinical

Other interesting facts:

- Alan Turing mentioned healthcare as one of the important applications of AI
- The LSA algorithm for factor analysis was developed by psychologists in the 1990s: A solution to Plato's problem: The latent semantic analysis theory of acquisition, induction, and representation of knowledge.

History of BioMedical NLP - biomedicine

1982:

GenBank - earliest genomic database

1990s: changes in the way biological scientists worked, with advances in genomics and bioinformatics - now can analyze 10,000s genes in one experiment (instead of one).

=> need to identify patterns and organize data

need to automatically analyze published papers (NLP) in order to identify new findings and populate gene databases

building massive databases of all known genes in multiple organisms + gene function

History of BioMedical NLP - biomedicine

1998:

earliest paper on biological text mining (*Fukuda et al 1998*, *Blaschke et al 1999*, *Craven & Kumlien 1999*)

- named entity recognition,
- rule-based information extraction,
- machine learning based information extraction
- automatic knowledge base construction

History of BioMedical NLP - biomedicine

The first attempts were developed by biologists and not aligned with latest advances in NLP

"**Model organism databases**" - repositories of facts about specific genes for species of interest - they were driving information extraction from biomedical literature

e.g.

- MedMiner (1999, published in Biotechniques): literature exploration of gene-drug and gene-gene relationships (based on GeneCard + extracted from PubMed/MEDLINE);
- iHOP (2004) organized literature around gene/protein of interest (Hoffman & Valencia 2004);
- Textspresso (2004) linked gene names in papers to WormBase entries (Muller, Kenny & Sternberg 2004, published in Bioinformatics);
- ARROWSMITH application for information extraction (Smalheiser & Swanson 1999) - "*a computer-assisted approach to formulating and assessing scientific hypotheses*"

Open questions & challenges

Unresolved issues around using **AI in clinical medicine** (from the beginning):

Societal

- workforce displacement
- skill atrophy
  Geoffrey Hinton: “*We should stop training radiologists now. It's just completely obvious that within five years, deep learning is going to do better than radiologists.*”

Ethical & legal

- algorithmic and user bias
- patient privacy
- medical-legal responsibility

Open questions & challenges

Unresolved issues around using **AI in clinical medicine** (from the beginning):

Practical

- oversight and regulations
- deployment into existing informatical systems can be problematic

Algorithmic

- *little* data, *missing* data, data shift, label *shift*, ... => semi-supervised methods, discovery
- needs to be robust