Machine Learning for Drug Discovery Research Literature Mining

We are interested in applications of machine learning to mine the research literature for additional types of entities/classes/answers relevant to drug discovery not already available to Open Targets which include but are not limited to variants, biomarkers, tissues/cell types, adverse events, and assay conditions.

Tasks

In this, you will need to develop an ML pipeline that involves:

1. Data Collection
2. Data Preprocessing (Visualization)
3. ML Model Development
4. Evaluation
5. Complexity of Models in Production

Note:

This notebook contains code for collecting the dataset and preprocessing (Tasks 1 and 2). The dataset we designed from tasks 1 and 2 in this notebook is for a named entity recognition problem. You are welcome to use this code and modify it as you please. Alternatively, you could also use free-to-use publicly available datasets or collect your own data solve train an ML model to solve a classification or a Q&A types of problem. *So, please feel free to develop your custom dataset and work towards prototyping an ML model to identify the aforementioned entities/ or build your own custom-designed classes and solve a classification problem of relevance/ or any of the answers of relevance.*

Important things to consider:

- Please use free Google Colab or Kaggle if you require GPU access.
- This task should not take more than 6 hours to solve.
- Achieving more than 60% F-score/accuracy on the dataset is *not a requirement*, and you are assessed based on the design choices and data science protocols you follow in solving this task.
- Once completed, please share your notebook as a zip file as *<firstname_lastname.zi>"*, including outputs and detailed comments.
- Feedback will be given on your notebook.

FalconFrames Environment Setup

This guide will walk you through setting up the Python environment and installing the necessary libraries for the test.

Prerequisites

Before you begin, ensure you have Python installed on your system. Python 3.7 or later is recommended.

Setting Up the Environment

1. **Create a Python Virtual Environment:**

   Run the following command to create a new virtual environment named `falconframes_env` in your home directory.

   ```
   python -m venv ~/falconframes_env
   ```
2. **Activate the Virtual Environment:**

   Activate the virtual environment using the command below:

   ```
   source ~/falconframes_env/bin/activate
   ```

   > Note: On Windows, the activation command is different. Use `~/falconframes_env\Scripts\activate`.

Installing Dependencies

With the virtual environment activated, install the required libraries using `pip`:

```
pip install notebook
pip install matplotlib
pip install lxml
pip install ipywidgets
```

Jupyter Notebook Extensions

Enable the required Jupyter Notebook extensions:

```
jupyter nbextension enable --py widgetsnbextension
```

Installing SciSpacy

Install SciSpacy and its dependencies:

```
pip install scispacy
pip install https://s3-us-west-2.amazonaws.com/ai2-s2-
scispacy/releases/v0.5.3/en_core_sci_sm-0.5.3.tar.gz
```

Usage

After installation, you can start using Jupyter Notebook for the FalconFrames project. Ensure the virtual environment is activated whenever you work on the project.

Deactivating the Environment

When you're done, you can deactivate the virtual environment by running:

`deactivate`

In [19]:
```
# python -m venv ~/falconframes_env

# source ~/falconframes_env/bin/activate


# pip install notebook
# pip install matplotlib
# pip install lxml
# pip install ipywidgets

# jupyter nbextension enable --py widgetsnbextension

# pip install scispacy
# pip install https://s3-us-west-2.amazonaws.com/ai2-s2-scispacy/releases
```

Import libraries

In [18]:
```
import csv
import pandas as pd
from tqdm import tqdm
import concurrent.futures
import requests
from requests.compat import urljoin
import matplotlib.pyplot as plt
import glob
import os
import re
from bs4 import BeautifulSoup

from nltk.tokenize import sent_tokenize

# We will use scipacy for sentence segmentation and tokenisation
import spacy
nlp = spacy.load("en_core_sci_sm", disable=["tagger", "parser", "ner", "l
nlp.add_pipe("sentencizer")
```

Out[18]:
```
<spacy.pipeline.sentencizer.Sentencizer at 0x7f8436339240>
```

1. Data Collection

In this scenario, we will use the Europe PMC Annotations API to collect our dataset.

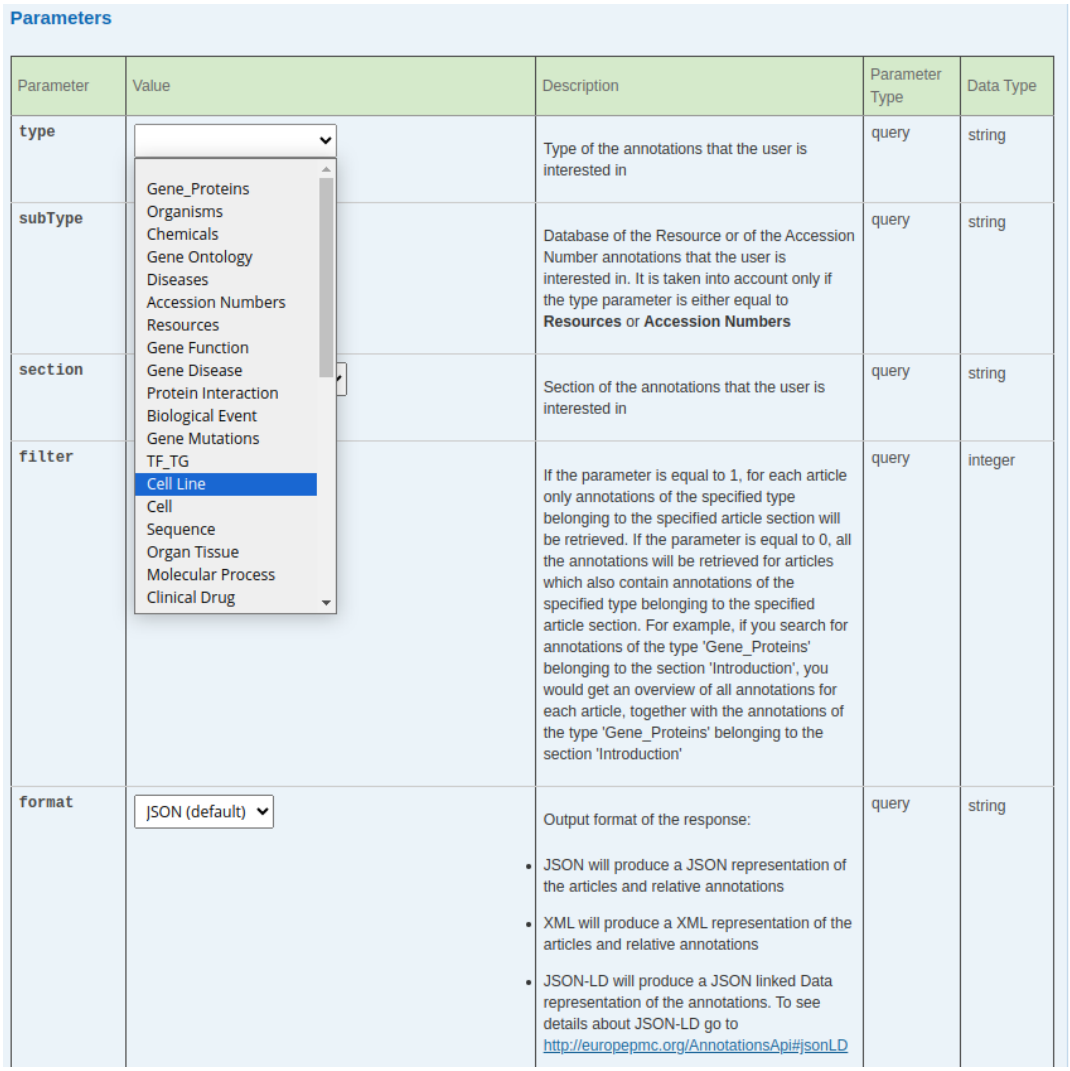
Please go to Europe PMC.

Click on the Developers -> Annotations API.

`GET /europepmc/annotations_api/annotationsBySectionAndOrType`

The types we are interested in for this particular task are:

- Gene Mutations (variants)
- Cell, Cell Line, and Organ Tissue (tissues/cell types)



Parameters

Parameter	Value	Description	Parameter Type	Data Type
type	Gene_Proteins Organisms Chemicals Gene Ontology Diseases Accession Numbers Resources Gene Function Gene Disease Protein Interaction Biological Event Gene Mutations TF_TG Cell Line Cell Sequence Organ Tissue Molecular Process Clinical Drug	Type of the annotations that the user is interested in	query	string
subType		Database of the Resource or of the Accession Number annotations that the user is interested in. It is taken into account only if the type parameter is either equal to **Resources** or **Accession Numbers**	query	string
section		Section of the annotations that the user is interested in	query	string
filter		If the parameter is equal to 1, for each article only annotations of the specified type belonging to the specified article section will be retrieved. If the parameter is equal to 0, all the annotations will be retrieved for articles which also contain annotations of the specified type belonging to the specified article section. For example, if you search for annotations of the type 'Gene_Proteins' belonging to the section 'Introduction', you would get an overview of all annotations for each article, together with the annotations of the type 'Gene_Proteins' belonging to the section 'Introduction'	query	integer
format	JSON (default)	Output format of the response: • JSON will produce a JSON representation of the articles and relative annotations • XML will produce a XML representation of the articles and relative annotations • JSON-LD will produce a JSON linked Data representation of the annotations. To see details about JSON-LD go to http://europepmc.org/AnnotationsApi#jsonLD	query	string

`CursorMark` : for pagination of the result list. For the first request, you can omit the parameter or use the default value 0.0. For every following page, use the value of the returned `nextCursorMark` element.

`PageSize` : 4


```
{
  "nextCursorMark": 5075.731130732,
  "cursorMark": 0,
  "articles": [
    {
      "source": "MED",
      "extId": "31211024",
      "pmcid": "PMC6555104",
      "annotations": [
        {
```

```
            "prefix": "ters\\n\\n\\nArthroplasty-",
            "exact": "Cervical",
            "postfix": "\\n\\nP001: Intravenous ",
            "tags": [
              {
                "name": "cervical region",
                "uri":
"http://purl.obolibrary.org/obo/UBERON_0005434"
              }
            ],
            "id":
"http://europepmc.org/article/PMC/PMC6555104#ontogene-
48929a03efe26120b761762f82fa795c",
            "type": "Organ Tissue",
            "section": "Article
(http://semanticscience.org/resource/SIO_001029)",
            "provider": "OntoGene"
          },
          // other annotations
        ]
      }
    ]
}
```


Using the nextCursorMark, we move forward collecting the datasets.

The exact is the entity we are interested in, and the prefix and postfix provide us with the context.

In [3]:
```
def get_epmc_annotations():
    base_url = "https://www.ebi.ac.uk/europepmc/annotations_api/annotatio
    types = ['Gene Mutations', 'Cell', 'Cell Line', 'Organ Tissue']
    data_list = []  # List to store the data

    for annotation_type in tqdm(types, desc="Processing Types"):
        cursor_mark = "0.0"
        for _ in range(2):  # Iterate 2 times for each type
            params = {
                'type': annotation_type,
                'filter': 1,
                'format': 'JSON',
                'cursorMark': cursor_mark,
                'pageSize': 4
            }
            response = requests.get(base_url, params=params)
            if response.status_code == 200:
                data = response.json()
                cursor_mark = data['nextCursorMark']

                for article in data['articles']:
                    pmc_id = article.get('pmcid')
                    if not pmc_id:
                        continue  # Skip this article if 'pmcid' is not f

                    for annotation in article['annotations']:
```

```
                        exact = annotation.get('prefix', '') + annotation
                        token = annotation['tags'][0]['name'] if annotati
                        ner = annotation['type']
                        data_list.append([pmc_id, exact, token, ner])
            else:
                print(f"Failed to fetch data for type {annotation_type} a

    annotations_df = pd.DataFrame(data_list, columns=['pmc_id', 'partial_
    return annotations_df
```

In [4]:
```
annotations_df = get_epmc_annotations()

rename_dict = {
    'Gene Mutations': 'GM',
    'Cell': 'CL',
    'Cell Line': 'CLine',
    'Organ Tissue': 'OT'
}

annotations_df['ner'] = annotations_df['ner'].map(rename_dict)
```

```
Processing Types: 100%|████████████████████████| 4/4 [00:17<00:00,  4.4
1s/it]
```

In [5]:
```
annotations_df
```

Out[5]:

	pmc_id	partial_sentence	token	ner
0	PMC3318213	arify the impact of H221Y mutation on drug re	H221Y	GM
1	PMC3318213	3 backbone plasmid. H221Y and (or) Y181C muta	H221Y	GM
2	PMC3318213	mid. H221Y and (or) Y181C mutations were reve	Y181C	GM
3	PMC3318213	cted, including the K101Q series (K101Q/Y181C	K101Q	GM
4	PMC3318213	g the K101Q series (K101Q/Y181C/H221Y, K101Q/	K101Q	GM
...	...	...	...	...
73128	PMC6849404	c disease involving vertebrobasilar circulatio...	vertebra	OT
73129	PMC6849404	th symptoms such as cortical blindness along wit	cortex	OT
73130	PMC6849404	ations which can be life threatening and dis	life cycle	OT
73131	PMC6849404	ning and disabling.\nCortical blindness, recoveri	cortex	OT
73132	PMC6849404	her symptoms after basilar artery stenting.\n...	basilar membrane of cochlea	OT

73133 rows × 4 columns

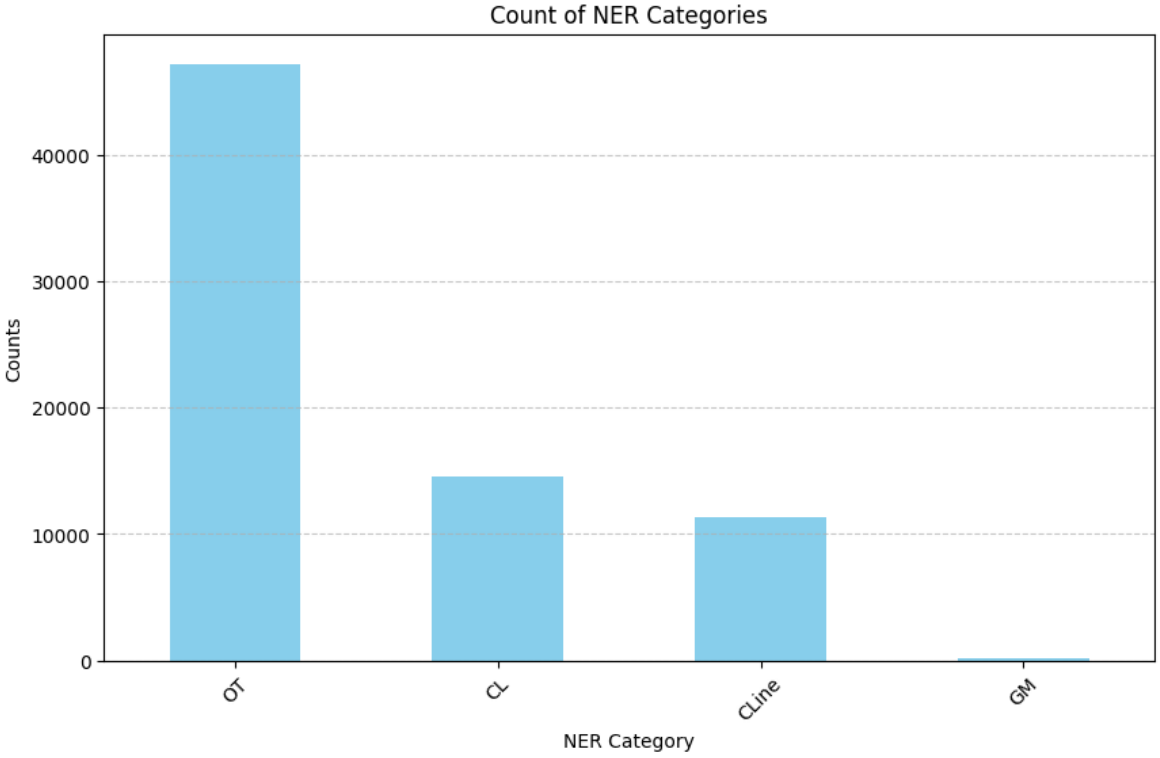
Check if the categerories are balanced?

In [6]:
```
ner_counts = annotations_df['ner'].value_counts()
print(str(ner_counts))

plt.figure(figsize=(10, 6))
ner_counts.plot(kind='bar', color='skyblue')

plt.title('Count of NER Categories')
plt.xlabel('NER Category')
plt.ylabel('Counts')
plt.xticks(rotation=45)
plt.grid(axis='y', linestyle='--', alpha=0.7)
```

```
ner
OT       47199
CL       14511
CLine    11290
GM         133
Name: count, dtype: int64
```



Create a balanced DataFrame where each ner type has an equal number of samples.

In [7]:
```
# def balance_ner_samples(df):
#     min_count = df['ner'].value_counts().min()
#     balanced_df = df.groupby('ner').apply(lambda x: x.sample(min_count)
#     return balanced_df

# balanced_annotations_df = balance_ner_samples(annotations_df)
```

In [20]:
```
# Determine the count of the least common ner type and then randomly samp
# This method fetches only 10 articles instead of 20 if we were to use th

def balance_ner_samples(df):
    min_count = df['ner'].value_counts().min()
    grouped = df.groupby('ner')
```

```
    selected_pmc_ids = set()
    balanced_df_list = []

    for name, group in grouped:
        # Try to select rows with pmc_ids already in selected_pmc_ids
        common_pmc_ids = group[group['pmc_id'].isin(selected_pmc_ids)]

        if len(common_pmc_ids) >= min_count:
            sample = common_pmc_ids.sample(min_count)
        else:
            remaining_count = min_count - len(common_pmc_ids)
            sample = pd.concat([common_pmc_ids, group[~group['pmc_id'].is

        selected_pmc_ids.update(sample['pmc_id'].tolist())
        balanced_df_list.append(sample)

    balanced_df = pd.concat(balanced_df_list).reset_index(drop=True)
    return balanced_df

balanced_annotations_df = balance_ner_samples(annotations_df)
```

In [21]:
```
balanced_annotations_df
```

Out[21]:

	pmc_id	partial_sentence	token	ner
0	PMC6833180	derived human CD34+ stem cells.\nFollowing eng...	stem cell	CL
1	PMC6833180	ecific mechanism of T cell evasion in AML\nShel	T cell	CL
2	PMC6833189	bone marrow-derived macrophages (BMDMs) and in...	macrophage	CL
3	PMC6833180	h peptide increased T cell infiltration in the	T cell	CL
4	PMC6833180	is also present on neutrophils, which represe...	neutrophil	CL
...	...	...	...	...
527	PMC6763540	10 years.\nSentinel nodes in 6 cases were neg	primitive knot	OT
528	PMC6763540	should be driven by gastric cancer histotype.\nP	mucosa of stomach	OT
529	PMC6854655	microstates, i.e., brain activity patterns,	brain	OT
530	PMC6854655	as the respiratory sinus arrhythmia (RSA), w	sinoatrial node	OT
531	PMC6763540	ells located in the lamina propria and muscula...	muscular coat	OT

532 rows × 4 columns

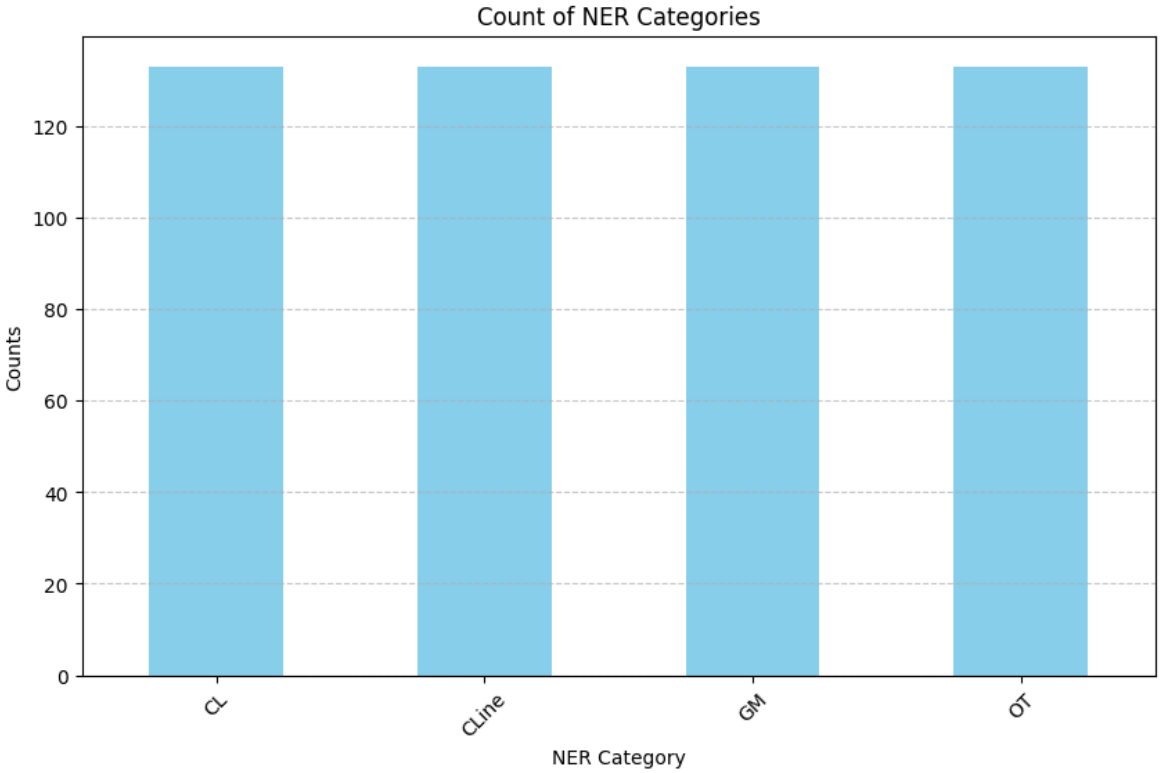
Check if the categerories are balanced?

In [10]:
```
ner_counts = balanced_annotations_df['ner'].value_counts()
print(str(ner_counts))

plt.figure(figsize=(10, 6))
ner_counts.plot(kind='bar', color='skyblue')
```

```
plt.title('Count of NER Categories')
plt.xlabel('NER Category')
plt.ylabel('Counts')
plt.xticks(rotation=45)
plt.grid(axis='y', linestyle='--', alpha=0.7)
```

```
ner
CL       133
CLine    133
GM       133
OT       133
Name: count, dtype: int64
```



In [11]:
```
unique_pmcids = balanced_annotations_df['pmc_id'].unique()
print(str(len(unique_pmcids)))
```

```
10
```

2. Data Preprocessing

However, we cannot train our dataset using just the context but need the whole sentence/paragraph. For this purpose, we use the Europe PMC Article API to fetch the article using the PMCID we obtained from the annotations API and extract the whole sentence from the context.

In [22]:
```
def get_relevant_paragraphs(pmcid, partial_sentences):
    relevant_paragraphs = []
    url = f"https://www.ebi.ac.uk/europepmc/webservices/rest/{pmcid}/full
    response = requests.get(url)
    if response.status_code == 200:
        soup = BeautifulSoup(response.content, 'lxml-xml')
        p_tags = soup.find_all('p')
```

```
        for tag in p_tags:
            paragraph_text = tag.get_text()
            if any(partial_sentence in paragraph_text for partial_sentenc
                relevant_paragraphs.append(paragraph_text)

        return relevant_paragraphs
    else:
        return None

def segment_sentences_spacy(text):
    doc = nlp(text)
    return [sent.text.strip() for sent in doc.sents]

def get_full_text_xml_paragraphs(pmcid, partial_sentences):
    segmented_sentences = []
    relevant_paragraphs = get_relevant_paragraphs(pmcid, partial_sentence

    if relevant_paragraphs:
        with concurrent.futures.ThreadPoolExecutor() as executor:
            # Map the segment_sentences function to each paragraph
            results = executor.map(segment_sentences, relevant_paragraphs

            for sentences in results:
                segmented_sentences.extend(sentences)

    return segmented_sentences

def find_sentence_with_substring(string_list, substring):
    for text in string_list:
        sentences = re.split(r'(?<=[.!?])\s+', text)
        for sentence in sentences:
            if substring in sentence:
                return sentence
    return None

def process_pmcid(df, pmcid, p_texts):
    sentences_data = {}
    for _, row in df[df['pmc_id'] == pmcid].iterrows():
        sentence = find_sentence_with_substring(p_texts, row['partial_sen
        if sentence:
            token = row['token']
            start_span = sentence.find(token)
            end_span = start_span + len(token)

            if start_span != -1:  # Ensure the token is found in the sent
                if sentence not in sentences_data:
                    sentences_data[sentence] = set()

                sentences_data[sentence].add((start_span, end_span, token

    return [[pmcid, sentence, list(ner_tags)] for sentence, ner_tags in s
```

In [23]:

```
# this is time consuming. The sentenciser takes 1 minute per article on a
final_data = []

for pmcid in tqdm(unique_pmcids, desc="Processing PMCIDs"):
    partial_sentences = annotations_df[annotations_df['pmc_id'] == pmcid]
    segmented_sentences = get_full_text_xml_paragraphs(pmcid, partial_sen
    processed_data = process_pmcid(annotations_df, pmcid, segmented_sente
    if processed_data:
```

```
        final_data.extend(processed_data)

# Convert to DataFrame
final_df = pd.DataFrame(final_data, columns=['pmcid', 'sentence', 'ner'])
```

```
Processing PMCIDs: 100%|██████████| 10/10 [09:47<00:00, 58.76s/it]
```

In [25]:
```
final_df.to_csv('final_df.csv', index=False)
```

In [26]:
```
final_df.sample(n=10)
```

Out[26]:

	pmcid	sentence	ner
5270	PMC6763540	\nObjective: ALK encodes a tyrosine kinase rec...	[(99, 103, lung, OT)]
2836	PMC6501469	Thus, we studied the effects of both polymorph...	[(70, 88, hippocampal neuron, CL)]
3500	PMC6854655	After applying our inference procedure to thes...	[(72, 86, pyramidal cell, CL)]
4356	PMC6854655	A two-part computational model has been develo...	[(68, 79, nerve fiber, OT)]
6650	PMC6763540	Experiments were conducted using suspension of...	[(47, 52, colon, OT), (54, 60, breast, OT)]
3684	PMC6854655	Electrical activity in cortical networks and t...	[(61, 67, neuron, CL)]
299	PMC6833180	The infiltration immune cells beyond T cells h...	[(37, 43, T cell, CL)]
313	PMC6833180	RNAseq of tumor-associated myeloid cells was c...	[(61, 66, MC-38, CLine), (27, 39, myeloid cell...
2559	PMC6833189	Studies have identified C-C Motif Chemokine Li...	[(54, 58, CCL4, CLine)]
3963	PMC6854655	Integrate-and-fire neuron models are widely us...	[(19, 25, neuron, CL)]

split the dataset into train, dev, and test.

Please train the dataset with selected your parameters and evaluate it on the dev set. Once you are happy with your evaluation, then evaluate the performance on the test set.

In [27]:
```
from sklearn.model_selection import train_test_split
train_size = 0.7
test_dev_size = 0.3
dev_size = 0.5  # Half of the test_dev_size, i.e., 15% of the total

train_df, test_dev_df = train_test_split(final_df, train_size=train_size,
test_df, dev_df = train_test_split(test_dev_df, test_size=dev_size, rando
```

In [28]:
```
dev_df.sample(n=10)
```

Out[28]:

	pmcid	sentence	ner
1025	PMC6833180	Consequently, by reducing tumor hypoxia in viv...	[(84, 90, T cell, CL)]
4128	PMC6854655	A realistic large-scale model of the cerebellu...	[(37, 47, cerebellum, OT)]
1049	PMC6833180	Specifically, we show that tumor microenvironm...	[(84, 90, T cell, CL)]
5152	PMC6763540	We compare the values, b1 and b1/b0, of coloni...	[(54, 60, tissue, OT), (40, 45, colon, OT)]
6968	PMC6821132	However, these assumptions have rarely been te...	[(117, 126, astrocyte, CL)]
6196	PMC6763540	There were also foci of mucocele-like changes,...	[(83, 89, stroma, OT)]
5643	PMC6763540	Their presence may be due to displacement or s...	[(63, 69, thymus, OT)]
3710	PMC6854655	This framework can also be straightforwardly e...	[(160, 174, pyramidal cell, CL), (70, 76, neur...
4717	PMC6763540	The tumour cells had eosinophilic and oncocyti...	[(21, 31, eosinophil, CL)]
6978	PMC6821132	There is precedent for the notion that microgl...	[(70, 79, phagocyte, CL)]

Convert the collected dataset into ML trainable format.

In [ ]:

```
def find_sub_span(token_span, entity_span):
    if token_span[0] < entity_span[1] and token_span[1] > entity_span[0]:
        return max(token_span[0], entity_span[0]), min(token_span[1], ent
    return None

def convert2IOB(text, ner_tags):
    doc = nlp(text)
    tokens = [token.text for token in doc]
    token_spans = [(token.idx, token.idx + len(token.text)) for token in
    iob_tags = ['O'] * len(tokens)

    for entity in ner_tags:
        start, end, entity_token, entity_type = entity
        entity_flag = False
        for i, token_span in enumerate(token_spans):
            if find_sub_span(token_span, (start, end)):
                if not entity_flag:
                    iob_tags[i] = 'B-' + entity_type
                    entity_flag = True
                elif iob_tags[i] == 'O':
                    iob_tags[i] = 'I-' + entity_type
            else:
                entity_flag = False

    # Validate tag sequence
    for i in range(1, len(iob_tags)):
        if iob_tags[i].startswith('I-') and iob_tags[i-1] == 'O':
            raise ValueError(f"Invalid tag sequence: 'I-' tag follows 'O'
```

```
    return list(zip(tokens, iob_tags))

def process_df_and_write(df, writer):
    for index, row in tqdm(df.iterrows(), total=df.shape[0], desc="Proces
        text = row['sentence']
        ner_tags = row['ner']  # assuming ner column is a list of tuples
        iob_pairs = convert2IOB(text, ner_tags)
        for token, tag in iob_pairs:
            writer.writerow([token, tag])
        writer.writerow('')
```

In [ ]:
```
with open('train.tsv', 'w', newline='\n') as f1, \
     open('dev.tsv', 'w', newline='\n') as f2, \
     open('test.tsv', 'w', newline='\n') as f3:
    train_writer = csv.writer(f1, delimiter='\t', lineterminator='\n')
    dev_writer = csv.writer(f2, delimiter='\t', lineterminator='\n')
    test_writer = csv.writer(f3, delimiter='\t', lineterminator='\n')

    # Process each DataFrame and write to the corresponding file
    process_df_and_write(train_df, train_writer)
    process_df_and_write(dev_df, dev_writer)
    process_df_and_write(test_df, test_writer)
```

3. ML Learning Model Development

There is liberty in using any model you would like e.g., Classification or Question and Answering. However, the dataset here provides an NER task for ML training.

In [ ]:
```
```

4. Evaluation

In [ ]:
```
#tip: hyperparameter tuning
```

5. Complexity

In [ ]:
```
# tip: model compression or knowledge distillation to remove complexity i
```