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Fine-tuning Pre-trained Transformer Language Models for Biomedical Event Trigger Detection

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Introduction

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- A biomedical event contains an event trigger and one or more arguments;
    - Event triggers generally refer to nouns or verbs that express a circumstance, process or eventuality.
    - Arguments refer to biomedical entities or other events.

Biomedical event extraction: Definition

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- **Argument word**: ‘O3’
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- **Role**: Theme

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Event 2 - *Regulation*

- **Trigger word**: ‘mediated’
- **Trigger category**: Regulation
- **Argument word 1**: *Event 1*
- **Role 1**: Theme
- **Argument word 2**: ‘aMT6s’
- **Argument category 2**: G_or_G_P
- **Role 2**: Cause

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- Event trigger detection identifies and classifies the event triggers into a set of predefined categories of events.
    - It has a critical role in building events, since the triggers are the targets that allow the construction of an event.
    - More than 60 % of biomedical event extraction errors occur in this sub-task [8].

Event trigger detection is challenging!

- The same event can be represented in the form of different expressions;
  - '[...] the mechanism that activates$_{+Reg}$ infiltrating macrophages [...]'
  - '[...] a limited role in post-ischemic macrophage activation$_{+Reg}$.'
  - '[...] antibodies that activated$_{?}$ inflammatory cytokine expression.'

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  - '[...] antibodies that activated$_{?}$ inflammatory cytokine expression.'

- They can be represented as single words or multi-words;
  - '[...] the neuroprotective efficacy$_{-Reg}$ of epigallocatechin-3-gallate (EGCG) [...]'
  - '[...] TLR4/NF-B pathway in LPS+A-induced$_{+Reg}$ rat microglia [...]'

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- They can present in-domain language or not;
  - '[...] Noncanonical Inflammasome via TLR4/NF-B Pathway$_{Pathway}$.'
  - '[...] and Neurotoxicity$_{Carcinogenesis}$ by Suppressing the Activation of Inflammasome'.
  - 'EGCG attenuates$_{_Reg}$ microglial inflammation [...]'

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  - 'EGCG attenuates$_{_Reg}$ microglial inflammation [...]'

- The same word can represent a different event according to the context (or the manual annotation?);
  - 'Anti-Survival and Pro-Apoptotic Effects$_{Reg}$ of 6-Shogaol [...]'
  - '[...] has anticancer effects$_{_Reg}$ on many types of tumors'.

Biomedical event trigger detection: Techniques

- Neural networks have been widely adopted for event trigger detection since they do not require the design of functions or use additional tools for their training.

- Models pre-trained on transformers architectures are commonly used for solving NLP tasks due to their positive achievements in performance.

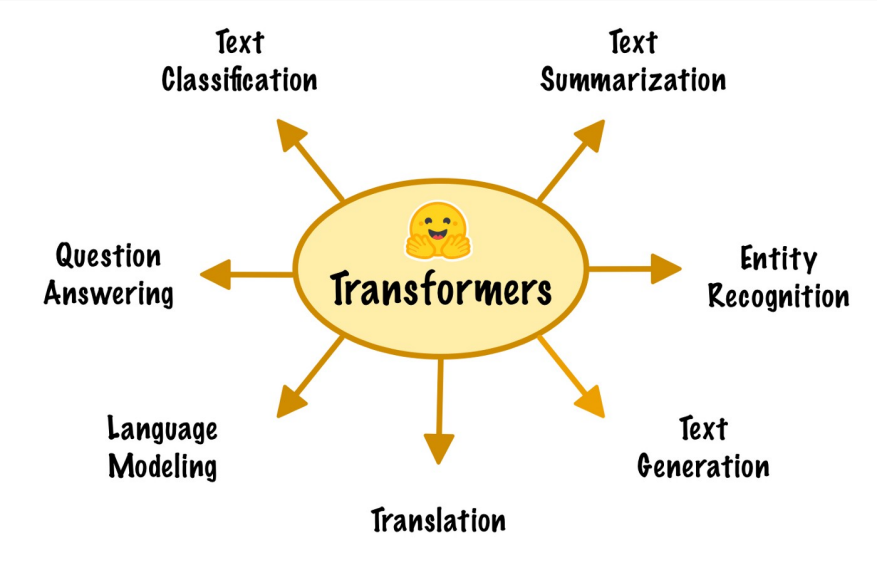
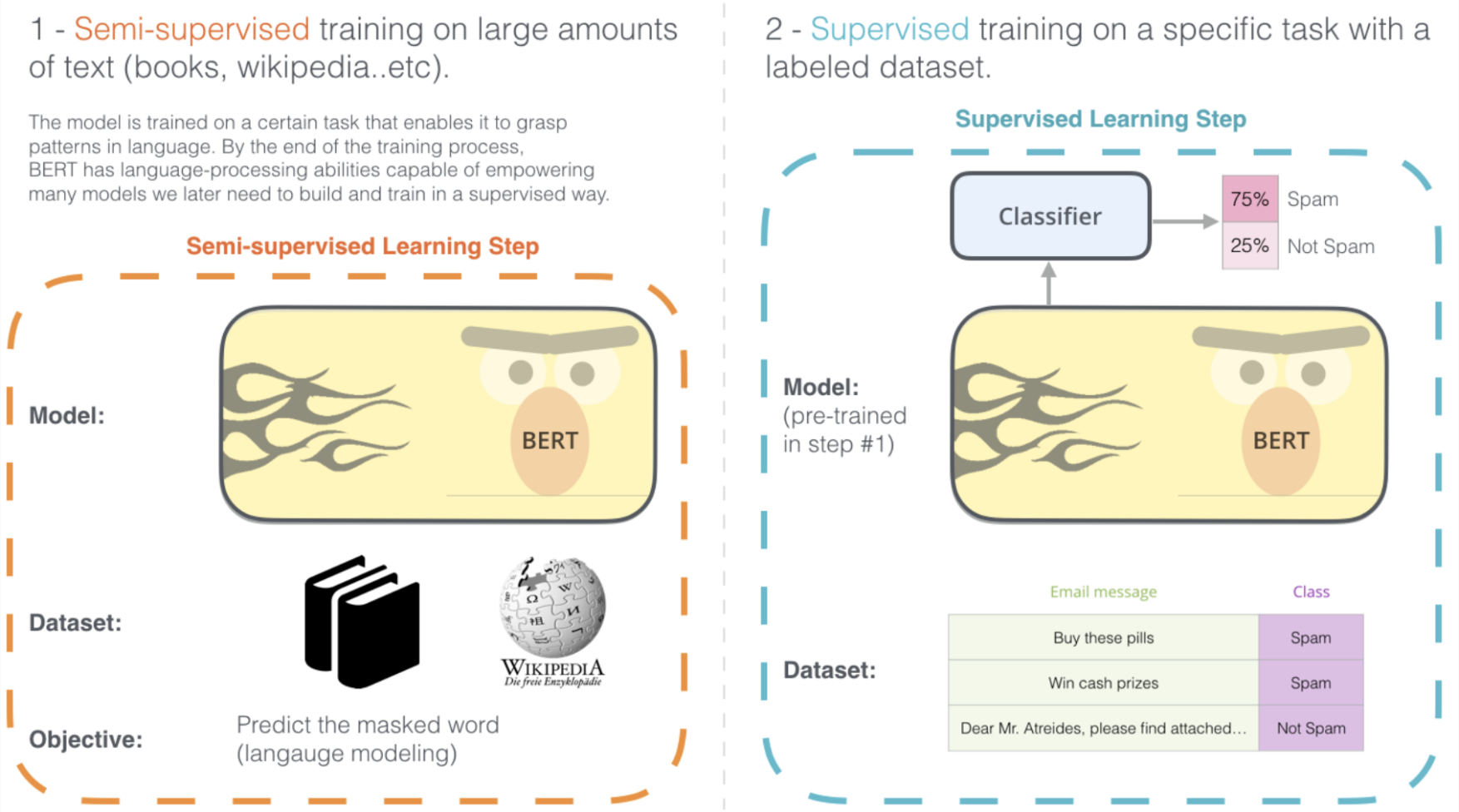


Figure obtained from: https://towardsdatascience.com/transformers-implementing-nlp-models-in-3-lines/-of-code-475639c3611d

Bidirectional Encoder Representations from Transformers



- BERT variants in the biomedical domain: BioBERT, PubMedBERT, BioMedRoBERTa, among others.

Figure obtained from `https://jalammar.github.io/illustrated-bert/`.

Work proposal and Contributions

This work compares five transformer language models (BERT, BioBERT, SciBERT, PubMedBERT and BioMedRoBERTa) for detecting biomedical event triggers using seven merged biomedical datasets to identify which model is the most appropriate for tackling this task;

Work proposal and Contributions

This work compares five transformer language models (BERT, BioBERT, SciBERT, PubMedBERT and BioMedRoBERTa) for detecting biomedical event triggers using seven merged biomedical datasets to identify which model is the most appropriate for tackling this task;

1. Identify whether using a transformer model pre-trained on the biomedical domain language presents advantages in performance.

2. Analyze whether using different biomedical corpus together for the models' training can improve event triggers detection.

Methods

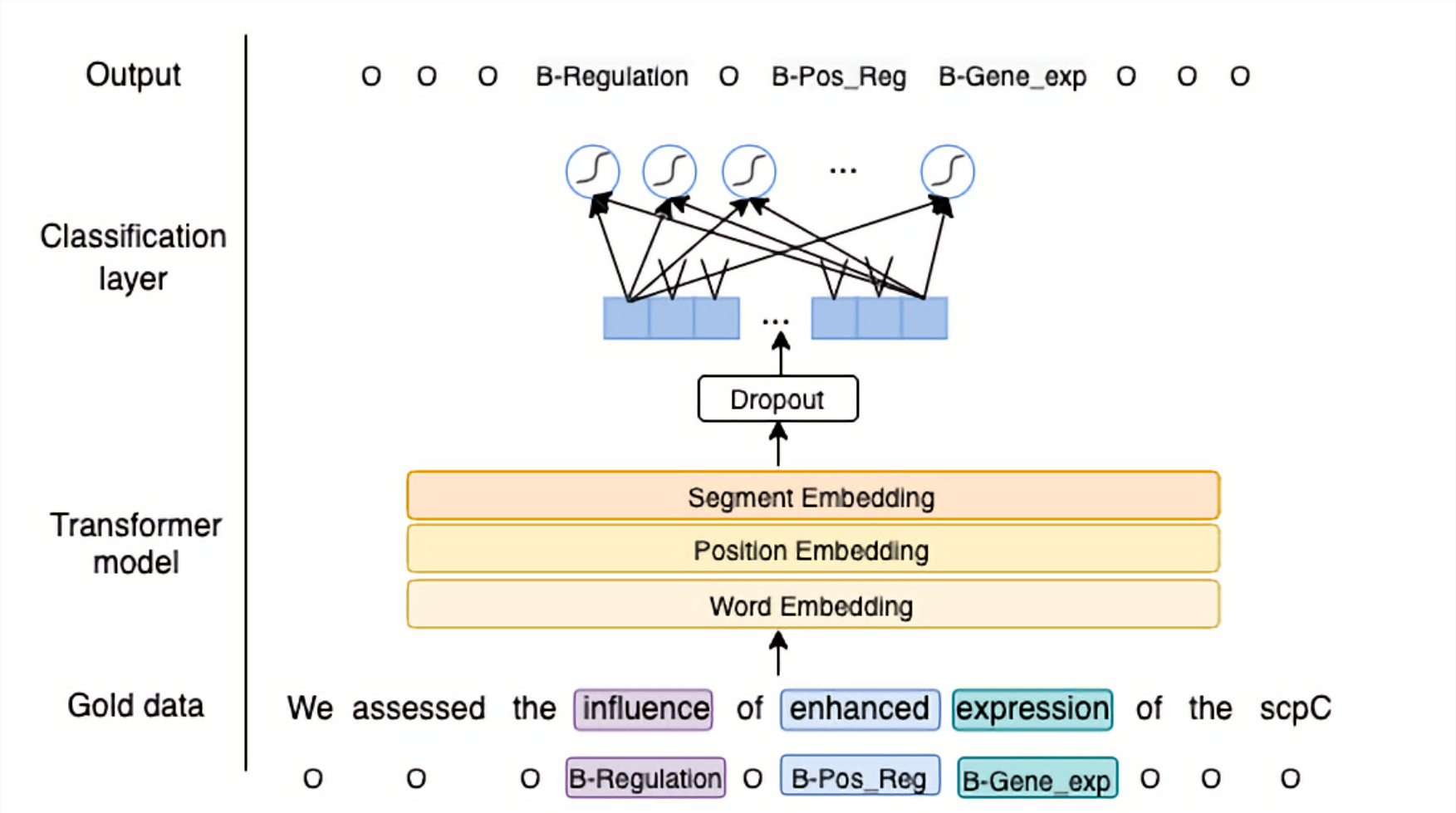
Detection of biomedical event triggers

The detection of biomedical event triggers can be considered as a multi-class problem;

IOB (Inside-Outside-Beginning) annotation of event triggers

‘PTHrP	**drives**	breast	tumor	**initial**	**progression**	and	**metastasis** ...’
‘O’	*‘B-Regulation’*	*‘O’*	*‘O’*	*‘B-Development’*	*‘I-Development’*	*‘O’*	*‘B-Metastasis’*

Model proposal



Experimental settings and Evaluation

Statistics of the corpus

Dataset	No. Triggers	No. Events	Documents	Train/Dev/Test
CG 2013	9,790	17,248	PubMed abstracts	300/100/200
EPI 2011	2,035	2,453	PubMed abstracts	600/200/400
GENIA 2011	10,210	13,560	MEDLINE abstracts	1,000 (total)
GENIA 2013	4,676	6,016	PMC full-text	34 (total)
ID 2011	2,155	2,779	PMC full-text	15/5/10
PC 2013	6,220	8,121	PubMed abstracts	260/90/175
MLEE	5,554	6,677	PubMed abstracts	131/44/87

- Total train and test sets: 19,855 and 4,964 sentences.
- Total trigger classes: 58.

Pre-trained language models

Model	Pre-training	Corpus
BERT	from scratch	WikiPedia + BookCorpus
BioBERT	from BERT	PubMed
SciBERT	from scratch	PMC* + Semantic scholar
PubMedBERT	from scratch	PMC* + PubMed
BioMedRoBERTa	from BERT	Semantic scholar

- Each model was fine-tuned for 10, 30 and 100 epochs.
- Precision, Recall and F1-score were measured for evaluation.

*PMC = PubMed Central

Evaluation of pre-trained models fine-tuned for trigger detection

Model	10 epochs			30 epochs			100 epochs		
	P	R	F1	P	R	F1	P	R	F1
BERT	**0.57**	**0.67**	**0.62**	**0.60**	**0.68**	**0.64**	0.62	0.68	0.65
BioBERT	0.51	0.61	0.55	0.57	0.59	0.58	**0.72**	**0.75**	**0.73**
SciBERT	0.59	0.64	0.61	0.61	0.65	0.63	0.70	0.70	0.70
PubMedBERT	0.49	0.61	0.54	0.58	0.66	0.61	0.58	0.62	0.60
BioMedRoBERTa	0.48	0.49	0.47	0.52	0.52	0.51	0.55	0.50	0.52

Category grained evaluation (BioBERT - 100 epochs)

Trigger category	P	R	F1	Support	Trigger category	P	R	F1	Support
Amino_acid_catabolism	1.00	1.00	1.00	1	Entity	0.63	0.74	0.68	398
Glycolysis	1.00	0.90	0.95	10	Degradation	0.68	0.68	0.68	19
Acetylation	0.86	0.99	0.92	82	Transcription	0.65	0.70	0.67	175
Phosphorylation	0.89	0.94	0.91	207	Synthesis	1.00	0.50	0.67	2
Deglycosylation	0.83	1.00	0.91	5	Conversion	0.55	0.75	0.64	28
Process	0.84	0.96	0.90	136	Regulation	0.66	0.57	0.61	556
Deacetylation	0.81	1.00	0.90	13	Blood_vessel_development	0.52	0.72	0.60	18
Metastasis	0.84	0.92	0.88	53	Transport	0.62	0.54	0.59	42
Methylation	0.85	0.90	0.87	73	Planned_process	0.65	0.54	0.59	104
Demethylation	0.75	1.00	0.86	3	Metabolism	0.57	0.57	0.57	7
Ubiquitination	0.82	0.90	0.86	67	Cell_death	0.56	0.58	0.57	43
Gene_expression	0.82	0.88	0.85	754	Growth	0.50	0.67	0.57	3
Hydroxylation	0.82	0.85	0.84	27	DNA_demethylation	0.40	1.00	0.57	2
Glycosylation	0.81	0.84	0.82	67	DNA_domain_or_region	0.57	0.57	0.57	7
DNA_methylation	0.82	0.82	0.82	77	Development	0.49	0.54	0.51	39
Cell_differentiation	0.92	0.73	0.81	15	Dephosphorylation	0.33	1.00	0.50	1
Carcinogenesis	0.78	0.81	0.79	31	Deubiquitination	1.00	0.33	0.50	3
Activation	0.78	0.80	0.79	65	Inactivation	0.44	0.53	0.48	15
Protein_catabolism	0.70	0.87	0.78	30	Catalysis	0.38	0.56	0.45	16
Pathway	0.79	0.76	0.78	168	Breakdown	0.40	0.50	0.44	4
Cell_proliferation	0.77	0.73	0.75	37	Mutation	0.45	0.41	0.43	32
Binding	0.72	0.79	0.75	434	Protein_processing	0.25	1.00	0.40	1
Negative_regulation	0.71	0.79	0.75	586	Anaphora	0.23	0.14	0.18	49
Localization	0.71	0.77	0.74	164	Protein_domain_or_region	0.00	0.00	0.00	5
Infection	1.00	0.56	0.71	9	Cell_division	0.00	0.00	0.00	2
Cell_transformation	0.76	0.67	0.71	39	Catabolism	0.00	0.00	0.00	5
Positive_regulation	0.72	0.68	0.70	1,276	Remodeling	0.00	0.00	0.00	1
Dissociation	0.64	0.78	0.70	9	Translation	0.00	0.00	0.00	2
Death	0.69	0.69	0.69	16	Dehydroxylation	0.00	0.00	0.00	1

Examples of ambiguous event triggers in gold data

‘When the dickkopf protein (Dkk) binds to Kremen and LRP5, this last **undergoes internalization and therefore becomes unable to bind Wnt**; this leads to degradation of beta-catenin and to inhibition of bone formation’.

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(annotation from gold data)

- The model incorrectly classified ***becomes*** as 'Regulation'.

Examples of ambiguous event triggers in gold data

'On the other hand, stimulation of T cells with mAb 9.3 increased the level of intracellular Ca2+ and triggered the activation of p56 (lck) and c-Raf-1, but **was unable to induce the binding of transcription factors to the IL-2** promoter.'

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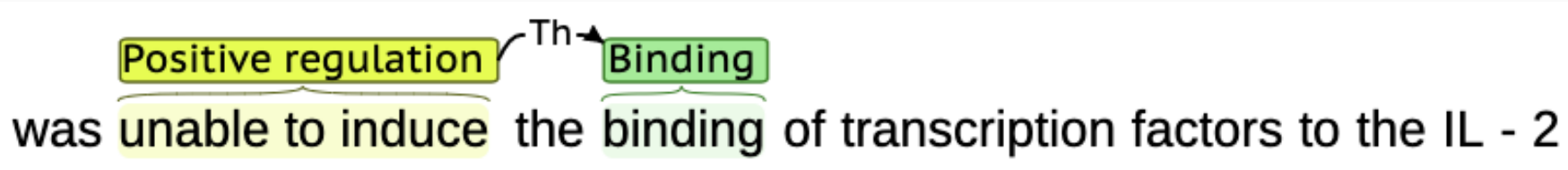

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- The model incorrectly classified ***unable to induce*** as 'Negative regulation'.

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‘Thus, Egr-2, in addition to Egr-3, regulates FasL expression in activated normal T cells, and Egr-2 is **likely to play a direct role in aberrant fasL up-regulation in lpr/lpr** and gld/gld CD4(-)CD8(-)T cells.’

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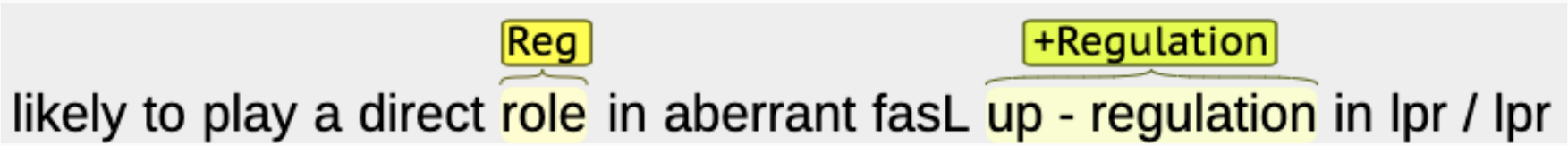

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- The model correctly classified ***role*** as 'Regulation'.

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‘By using PD-98059 and SB203580, two potent and selective inhibitors of MEK1 and p38, respectively, we have demonstrated that both **ERK1/2 and p38 cascades play a key role in the production of IL-8** by monocytes and PMN stimulated with bacterial fractions.’

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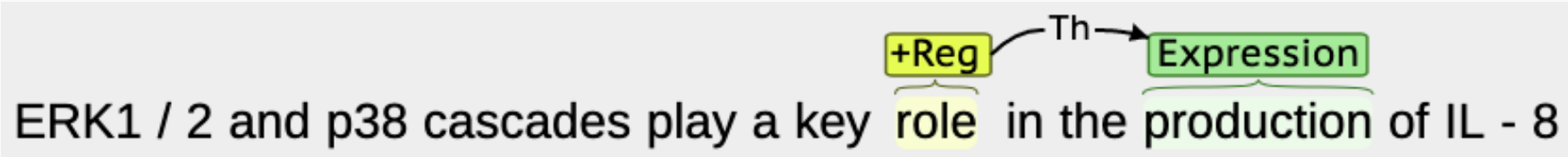

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Conclusions and Future work

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- BioBERT presents the highest performance in detecting biomedical event triggers when it is trained during 100 epochs.
    - This result suggests that a model pre-trained on biomedical data that starts its pre-training from BERT weights is the best strategy for biomedical event trigger detection.
- Using different corpus merged as input data can enrich event detection, since they provide more trigger categories and samples to train the model.
- However, the categories of triggers with high number of samples do not necessarily present high performance.
    - These results suggest that the triggers samples may present ambiguities, making it difficult for the model to achieve the generalization, even if the number of samples is relatively significant.

Future work

For the next steps:

- to enrich the information given to the model by adding extra features, as the Parts-Of-Speech [4] or the syntactic dependency path [8], to reduce ambiguities;

- to merge the trigger categories with the lowest support to other categories with similar events to reduce the imbalance of the data.

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References I

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