ISSN No:-2456-2165 https://doi.org/10.5281/zenodo.14603421

Exploring Causal Relationships in Biomedical Literature: Methods and Challenges

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Abstract:- The extraction of causal relationships from biomedical literature, focusing on overcoming the unique challenges presented by the complexity of biomedical language, implicit causalities, and the scarcity of large annotated datasets. The research offers an extensive review of various methods, ranging from rule-based systems to classical machine learning models such as SVMs, to the cutting-edge deep learning techniques including LSTM, CNN, and BioBERT, which have significantly improved the identification of both explicit and implicit causal relationships. A major contribution of this work lies in addressing the limitations posed by small datasets through the incorporation of semi-supervised learning and data augmentation techniques. The paper also emphasize the importance of capturing temporal dependencies to enhance the understanding of event sequences, crucial for recognizing causality in biomedical studies. Furthermore, the research underscores the significance of domain adaptation, fine-tuning general-purpose datasets like SemEval for the specific needs of biomedical literature, which often contains domain-specific terms and complex structures. By tackling these challenges and proposing innovative solutions, this paper advances the field of biomedical text mining, offering valuable insights for future research and practical applications in clinical decision support, drug safety monitoring, and biomedical knowledge discovery.

Keywords:- *Biomedical Causal Discovery; Biomedical Causality Mining; Causal Relationship Mining; Biomedical Text Analysis; NLP in Biomedical Research.*

I. INTRODUCTION

The extraction of causal relationships from biomedical texts has gained prominence due to its relevance in various biomedical applications, including drug discovery, disease treatment, and medical diagnostics. Biomedical literature contains intricate relationships between proteins, drugs, and diseases, which are essential for advancements in personalized medicine and clinical decision-making.

However, these texts are often complex, with ambiguous terminology and implicit relationships that make extracting causal links challenging [1], [2]. Traditional rule-based systems that rely on predefined patterns have limitations, particularly in their inability to adapt to new datasets and handle implicit relationships, which necessitates the development of more advanced methods [1], [3].

Machine learning and deep learning approaches have become pivotal in overcoming these limitations. Techniques such as Convolutional Neural Networks (CNNs) [4] and Recurrent Neural Networks (RNNs) [5], especially Long Short-Term Memory (LSTM) [6] networks, have been employed to extract causal relations from biomedical texts more efficiently than traditional systems. These models capture the context of relationships within sentences and have demonstrated improved scalability and flexibility. BERT and its domain-specific variant, BioBERT, are particularly notable for their ability to capture local and global dependencies, enhancing performance in tasks related to causality extraction [7], [8], [9].

Despite these advancements, several challenges remain. Biomedical texts often involve implicit relationships, where causal connections are inferred rather than explicitly stated. Additionally, the lack of large annotated biomedical datasets hinders the training of robust machine learning models. This scarcity necessitates the use of data augmentation techniques, semi-supervised learning, and domain-specific model adaptations to overcome the challenges posed by limited datasets. The adaptation of general-purpose models like SemEval [10] for biomedical tasks further highlights the need for more tailored approaches in this domain [11], [12], [13].

Table 1 Examples of Implicit Causality in Biomedical Texts

Connectives	Sentences	Labels
“due to”	The patient’s fever subsided due to the antipyretic medication [1].	Causal
“resulting from”	There was a significant reduction in symptoms resulting from the therapy [1].	Causal
“even though”	Even though the treatment was administered, the patient’s condition worsened [14].	Non-causal
“thereby”	The drug reduced inflammation, thereby improving patient recovery [15].	Causal
“despite”	Despite the positive initial response, complications arose later [16].	Non-causal
“following”	Following the surgery, the patient experienced mild swelling [17].	Causal

ISSN No:-2456-2165 https://doi.org/10.5281/zenodo.14603421

This table-1 provides examples of connectives in biomedical contexts, showcasing how they can imply causal or non-causal relationships. The relevance of this table is illustrating the complexity of biomedical text, where connectives like "due to," "despite," and "thereby" play crucial roles in expressing causality. Understanding these patterns is key to improving the accuracy of causality extraction models in biomedical literature.

The methods of the investigations and challenges associated with extracting causality from biomedical texts. The research work focuses on improving the accuracy of causal relationship extraction through advanced deep learning models and propose innovative solutions to handle language complexity, dataset limitations, and implicit relationship extraction.

By addressing these challenges, the contributions aim to enhance the field of biomedical text mining, enabling more effective analysis of biomedical literature for applications in research and clinical settings [18], [19].

Furthermore, this research lays the groundwork for future developments in causality extraction, emphasizing the importance of enhancing domain-specific models and expanding high-quality biomedical datasets to support ongoing advancements in this area [20], [21], [22].

II. TYPES OF CAUSAL RELATIONSHIPS IN BIOMEDICAL TEXT

Causal relationships in biomedical literature are central to understanding how various factors such as treatments, diseases, symptoms, and patient outcomes interact. The ability to detect and extract these relationships is fundamental for applications like clinical decision-making, drug discovery, and knowledge graph creation. Causal relationships in biomedical texts can be classified into three main types: explicit, implicit, and inter-sentential relationships. Each type presents distinct challenges in extraction due to the complexity and nuances of natural language.

- *Explicit Causal Relationships*

Explicit causal relationships occur when the cause and effect are directly expressed within the text, typically signaled by clear causal markers such as "cause," "lead to," or "result in." These types of relationships are relatively simple to identify through rule-based methods or keyword spotting, as they present well-defined linguistic cues. For instance, in sentences like "Aspirin causes gastrointestinal bleeding" or "Taking Drug X leads to a significant decrease in blood pressure," the causal connections are explicitly stated, making them easier to detect. Models designed for rule-based methods and graph-based approaches have shown success in handling such explicit causal relationships [23], [24].

Despite their simplicity in extraction, explicit causal relationships tend to be less frequent in biomedical texts compared to implicit ones. While they offer a clear understanding of the causal links, the biomedical domain often presents more complex, nuanced interactions where the cause-effect relationship is implied rather than directly stated. Therefore, while rule-based extraction models perform well on explicit relationships, the need for advanced techniques is crucial to uncover implicit relationships, which are more common and critical in biomedical research [1], [3].

- *Implicit Causal Relationships*

Implicit causal relationships are those that are not directly stated within the text but require inference from the surrounding context. These relationships are more difficult to extract because the causal link between entities is implied rather than explicitly mentioned.

In biomedical literature, implicit relationships are particularly common, as drugs or treatments are often described alongside their effects without the use of explicit causal connectors. For instance, in sentences like "The patient took Drug X and subsequently experienced gastrointestinal bleeding" or "After undergoing chemotherapy, the patient's immune system weakened," the cause-effect connection is implied but not clearly stated, making extraction more challenging.

Extracting implicit relationships requires a deeper understanding of the context. Advanced techniques, such as deep learning models like BERT and SciBERT [25], [26], are increasingly being employed to capture these subtle contextual dependencies and infer the underlying causal connections. Additionally, neural models, such as CNNs and attention-based mechanisms [27], have shown effectiveness in extracting implicit relationships by focusing on the relationships between words and phrases within the broader text [7], [28]. These methods allow for the identification of nuanced causal links that are not easily detectable using traditional rule-based approaches.

- *Inter-Sentential Causal Relationships*

Inter-sentential causal relationships are more complex as they span across multiple sentences or even paragraphs, where the cause and effect may not be present within the same sentence. Instead, these relationships are distributed throughout the text, making it challenging to track and extract the causal link. In biomedical literature, these relationships often describe how treatments or drugs influence patient outcomes over time. For instance, "The patient was prescribed Drug X. Two days later, they began experiencing severe nausea" or "The patient received a new treatment for hypertension. Over the next few days, their blood pressure dropped significantly" illustrates how the cause (the treatment) and the effect (the outcome) are separated by several sentences, adding complexity to the extraction process [29].

To extract inter-sentential causal relationships effectively, advanced models that can handle long-range dependencies, such as LSTM networks or Transformer models, are required [30], [31]. These models are capable of retaining the context across multiple sentences, enabling them to detect causality that extends beyond sentence boundaries. Recent advancements, including the use of graph attention networks, have also shown significant promise in capturing these complex causal relationships [32].

ISSN No:-2456-2165 https://doi.org/10.5281/zenodo.14603421

By effectively modeling the relationships between different parts of the text, these models offer a more robust solution for extracting intersentential causal relationships in biomedical literature.

The comparison table-2 provided in this section outlines the key characteristics of the various types of causal relationships found in biomedical texts. It highlights examples for each type, such as explicit causal relationships that directly state cause and effect, versus implicit ones where the connection must be inferred. Inter-sentential relationships span across multiple sentences or paragraphs, requiring more advanced methods for detection.

Each type of relationship presents unique challenges for extraction, and the table summarizes these, along with the suitable techniques for identifying them, such as rule-based like LSTM or BERT for more complex cases.

Table 2 Comparison of Causal Relationship Types in Biomedical Text

Type	Characteristics	Example	Challenges in Extraction	Possible Extraction Methods
Explicit Causal Relationships	Cause and effect are directly stated with clear causal markers	*"Aspirin causes gastrointestinal bleeding"*	Easy to extract, but less frequent	Rule-based methods, graph kernels [24], [23]
Implicit Causal Relationships	Cause and effect are implied and must be inferred from context	*"The patient took Drug X and experienced nausea"*	Requires inference, ambiguous connections	Deep learning models (BERT, SciBERT), contextual embedding [25], [26]
Inter-Sentential Causal Relationships	Cause and effect are separated across sentences or paragraphs	*"Drug X was prescribed. Two days later, nausea occurred"*	Requires tracking con-text over multiple sentences	LSTM, Transformer models, graph-based models [30], [31], [32]
Temporal Causal Relationships	Events are ordered based on time, with causality inferred from temporal sequence	*"After administering Drug X, symptoms improved"*	Requires understanding temporal progression	Timeline modeling, temporal extraction [33]
Conditional Causal Relationships	Cause and effect occur only under specific conditions	*"If Drug X is taken with alcohol, it may cause liver damage"*	Subtle conditions, harder to detect	Conditional clause detection, advanced NLP parsing [23]

This table-2 serves as a quick reference to understand how these relationships differ in their presentation, complexity, and the models required for their accurate extraction.

In addition, Understanding and extracting causal relationships from biomedical literature is crucial for advancing fields such as drug discovery, clinical decision-making, and medical research. The identification of these relationships allows researchers to make better-informed conclusions regarding the effectiveness of treatments, the risks associated with certain drugs, and the underlying mechanisms of diseases.

This section lays out a comprehensive understanding of explicit, implicit, and inter-sentential causal relationships, their complexities, and the methodologies for extracting them. By breaking down these relationships and their extraction challenges, therefore, it provides a foundation for improving the efficiency and accuracy of Natural Language Processing (NLP) [34] tools in biomedical research, which is essential for the overall goal of this paper—enhancing automated systems in understanding biomedical literature.

III. DATASETS FOR CAUSALITY EXTRACTION IN MIOMEDICAL TEXT

Biomedical text is rich with causal relationships, whether they describe drug interactions, gene expressions, or adverse medical events. These relationships are critical for advancing medical research and clinical applications, making the accurate extraction of causality essential. Several datasets have been developed to support the extraction of these causal relationships, each with its own focus on different aspects of biomedical interactions.

Below, there are discussion about prominent datasets that used for causality extraction, their characteristics, and their relevance to biomedical research.

- *BioInfer*

BioInfer is a dataset that contains annotated relations between genes, proteins, and RNA, making it an excellent resource for studying interactions in molecular biology. BioInfer includes comprehensive information on how these entities influence each other, which is essential for understanding gene-disease path-ways.

The dataset also includes annotations of biological processes, which are pivotal in developing systems that can recognize and extract complex causal relationships in biological contexts [35]. The richness of BioInfer has made it a benchmark for various biomedical text mining tasks, including gene-disease interaction studies and pathway discovery.

- *ADE (Aderse Drug Events)*

The ADE dataset focuses on drug-disease interactions, specifically adverse events caused by pharmaceutical interventions [36]. ADE is one of the most crucial resources for pharmacovigilance, allowing researchers to identify causal links between drugs and side effects.

ISSN No:-2456-2165 https://doi.org/10.5281/zenodo.14603421

With over 6,000 sentences annotated with drug-disease relationships, this dataset helps in building models that detect adverse reactions, contributing to drug safety monitoring [37]. It is commonly used in the development of automated systems for identifying harmful drug effects from clinical reports and literature.

- *SemEval-2010 Task 8*

SemEval-2010 Task 8 is a widely used dataset for semantic relation classification. Although it is not exclusively biomedical, its flexibility allows it to be adapted for biomedical applications. The dataset contains a diverse set of relation types, including cause-effect, which can be applied to biomedical texts for causality extraction.

This general-purpose dataset helps in building models that are not only tuned for biomedical causality but can also be generalized to other domains [38]. Researchers frequently use SemEval-2010 Task 8 to train causality extraction models for broader NLP applications, which are later fine-tuned for specific biomedical tasks.

Table 3 Comprehensive Comparison of Biomedical Causality Extraction Datasets (SBC=Suitability for Biomedical Causality)

Dataset	Domain	Size	Relation Types	Data Structure	Applications	SBC
BioInfer	Biomedical	1,461 sentences	Gene, protein, RNA interactions	Sentences annotated with biological interactions	Gene-disease interaction studies, molecular pathways [35]	High
ADE	Biomedical	6,821 sentences	Drug-adverse event relations	Case reports, clinical text	Pharmacovigilance, drug safety monitoring [37]	High
SemEval-2010 Task 8	General (adaptable)	10,717 examples	Cause-effect, other semantic relations	Sentence pairs annotated with semantic relations	General NLP applications, adaptable to biomedicine [38]	Moderate
PDTB 2.0	General (WSJ)	9,190 discourse relations	Discourse-level causal relations	Annotated with explicit and implicit causal markers across texts	Discourse-level analysis, biomedical literature with discourse structures [40]	High
BioNLP Shared Task 2011	Biomedical	1,808 abstracts	Event and entity relationships	Structured abstracts and full-text annotations	Event extraction, gene regulation studies [41]	High
Causal Time-Bank	Mixed-domain	183 documents	Temporal and Causal relations between events	Annotated with cause-effect and time relations in text	Event-based causality extraction, adaptable to medical texts [42]	Medium
CHEMPROT	Biomedical	25,000 abstracts	Protein-chemical compound interactions	Abstracts from biomedical literature	Chemical-protein interaction studies, drug discovery [43]	High
GENIA	Biomedical	2,000 abstracts	Biological interactions	Abstracts with biological event annotations	Biological process modeling, gene regulation [44]	High

The table-3 provides a comprehensive comparison of several datasets that are commonly used for causality extraction in biomedical text. Each dataset is presented with details on its domain, size, and the types of relationships it captures, data structure, and its applications in various fields of biomedical research. BioInfer, ADE, and GENIA are specifically tailored for biomedical purposes, focusing on biological interactions, drug-adverse event relations, and protein-chemical interactions, respectively. Datasets like SemEval-2010 Task 8 and PDTB 2.0, although not initially designed for biomedical purposes, are adaptable and useful in training causality extraction models with additional fine-tuning. Each dataset is assessed for its suitability for biomedical causality research, where most of them demonstrate high potential for application in this domain, despite some needing domain-specific customization.

- *PDTB 2.0 (Penn Discourse TreeBank)*

The Penn Discourse TreeBank (PDTB) 2.0 [39] is a comprehensive dataset that provides annotations for discourse-level relationships, including causality. PDTB 2.0 is primarily based on the Wall Street Journal corpus but has found applications in biomedical discourse analysis due to its detailed causal relation annotations. It includes both explicit and implicit causal markers, making it suitable for analyzing complex biomedical texts where causality is spread across multiple sentences or paragraphs [40].

The table-4 highlights the advantages and limitations of the datasets discussed. For example, BioInfer provides rich annotations of gene-protein interactions but is limited to molecular biology, making it less generalizable. ADE is crucial for pharmacovigilance, focusing on drug safety, but lacks coverage of broader biomedical relations. SemEval-2010 Task 8, while versatile, requires adaptation for biomedical use. Each dataset offers unique strengths—some are ideal for discourse-level analysis, others for event extraction or chemical-protein interactions. However, many datasets face the challenge of being domain-specific or limited in scope, which may require additional annotation or extension to be fully useful for extracting biomedical causality relations.

ISSN No:-2456-2165 https://doi.org/10.5281/zenodo.14603421

Table 4 Advantages and Limitations of Biomedical Causality Extraction Datasets

Dataset	Advantages	Limitations
BioInfer	- Rich biological interaction annotations. - High relevance for genedisease pathway studies.	Focused on molecular biology interactions; not generalizable [35].
ADE (Adverse Drug Events)	- Rich annotations on Drug-adverse event relationships. - Essential for pharma-covigilance and drug safety.	Limited to adverse drug reactions, lacking broader biological relations [37].
SemEval-2010 Task 8	- Versatile dataset adaptable to multiple domains. - Strong for semantic relation classification.	Requires adaptation for biomedical causality extraction [38].
PDTB 2.0	- Ideal for discourse-level analysis of causal relations. - Annotates explicit an implicit causal markers.	General discourse dataset, not biomedical-specific [40].
BioNLP Shared Task 2011	- Broad entity-relation annotations, suitable for many biomedical fields. - Includes event extraction for complex biomedical processes.	Focuses on event extraction, less on direct causal relation extraction [41].
Causal-Time-Bank	- Addresses both temporal and causal event relationships. - Adaptable to biomedical texts.	Small dataset, mixed domain focus, limited to biomedical text [42].
CHEMPROT	- Large dataset with chemical-protein interaction annotations. - Key for drug discovery and chemical interaction studies.	Focused solely on Chemical-protein interactions, not broader causal extraction [43].
GENIA	- Detailed biological event annotations. - Useful for biological process modeling and gene regulation studies.	Limited to biological texts, not broadly applicable across all biomedical fields [44].

The key datasets relevant to causality extraction in biomedical texts, which form the backbone for developing effective computational models in this area. For further research, these datasets provide essential resources to train, evaluate, and fine-tune models aimed at identifying causal relationships in biomedical literature. Using these datasets allows for greater accuracy in tasks such as drug safety monitoring, gene-disease interaction studies, and discourse-level causal analysis. By selecting the most appropriate dataset based on the research focus that can ensure the models capture the nuanced relationships present in complex biomedical texts. This is crucial for improving the efficiency and precision of causality extraction methods, which form the foundation of the research objective.

IV. TECHNIQUES FOR CAUSALITY EXTRACTION IN BIOMEDICAL TEXT

In biomedical text mining, extracting causal relationships is crucial for understanding complex biological processes and interactions, which can lead to significant advancements in research and clinical applications. Various methods have been developed to extract causal relationships from text, including rule-based systems, machine learning, deep learning, and hybrid approaches. Each of these techniques has its own strengths and limitations, and in this section, a review of these approaches along with examples and tools used in the biomedical domain.

- *Rule-Based Systems*

Rule-Based Systems In this research, rule-based systems play a foundational role in extracting causal relationships from biomedical texts. These systems utilize predefined lexico-syntactic patterns to detect clear causal relationships, such as "Drug X causes Symptom Y," making them highly effective for handling explicit causal connections. They provide precision and interpretability, which are beneficial in scenarios where accuracy in detecting direct causal links is essential. However, the limitations of rule-based systems become evident when dealing with more complex biomedical literature, where implicit relationships or multi-sentence dependencies are common. Despite their effectiveness in structured data, the inflexibility and lack of adaptability to new patterns without manual reconfiguration remain major challenges [45].

- *Machine Learning Approaches*

The research highlights the benefits of classical machine learning models such as Support Vector Machines (SVMs) [46] and decision trees [47], which are widely used for causality extraction in biomedical texts. These models rely on carefully engineered features like syntactic structures [48], part-of-speech tags [49], and word embedding [50]. Machine learning approaches are more adaptable compared to rule-based methods [51], allowing for greater flexibility when dealing with various types of biomedical texts. However, these models still face limitations in handling implicit causal relationships that require deeper contextual understanding. Moreover, the success of these approaches depends on the quality of feature engineering, which often requires domain-specific knowledge [25]. Machine learning methods also struggle with causal links spread over multiple sentences, highlighting the need for more advanced models [26].

- *Deep Learning Approaches*

Deep learning models have revolutionized causality extraction in recent years, and the research underscores the importance of models such as LSTM networks, CNN, and transformers like BERT and BioBERT. These models can learn complex patterns in data, allowing them to extract both explicit and implicit causal relationships without manual feature engineering. BERT, for example, has been pre-trained on large biomedical corpora and fine-tuned to handle nuanced

ISSN No:-2456-2165 https://doi.org/10.5281/zenodo.14603421

relationships within biomedical texts [52]. Therefore, the research demonstrates that deep learning models are particularly effective in capturing intersentential causal relationships and understanding the broader context in biomedical literature. However, these models require large annotated datasets for training and significant computational resources, which can limit their application in resource-constrained environments [26].

➢ *Hybrid Approaches*

In this research, hybrid approaches are proposed as a solution to overcome the limitations of both rule-based and machine learning methods by combining their strengths. Hybrid systems leverage the precision of rule-based approaches for detecting explicit causal links, while utilizing machine learning and deep learning models for handling more complex or implicit relationships. This combination allows for higher accuracy and adaptability, making hybrid models particularly useful in extracting causal relationships from biomedical texts where data variability is high.

Hybrid models also perform well when dealing with limited annotated datasets, where rule-based methods can provide reliable baselines while deep learning models handle more intricate patterns [53]. Despite these advantages, hybrid approaches come with increased system complexity, requiring careful integration and balancing between different models to optimize performance [54].

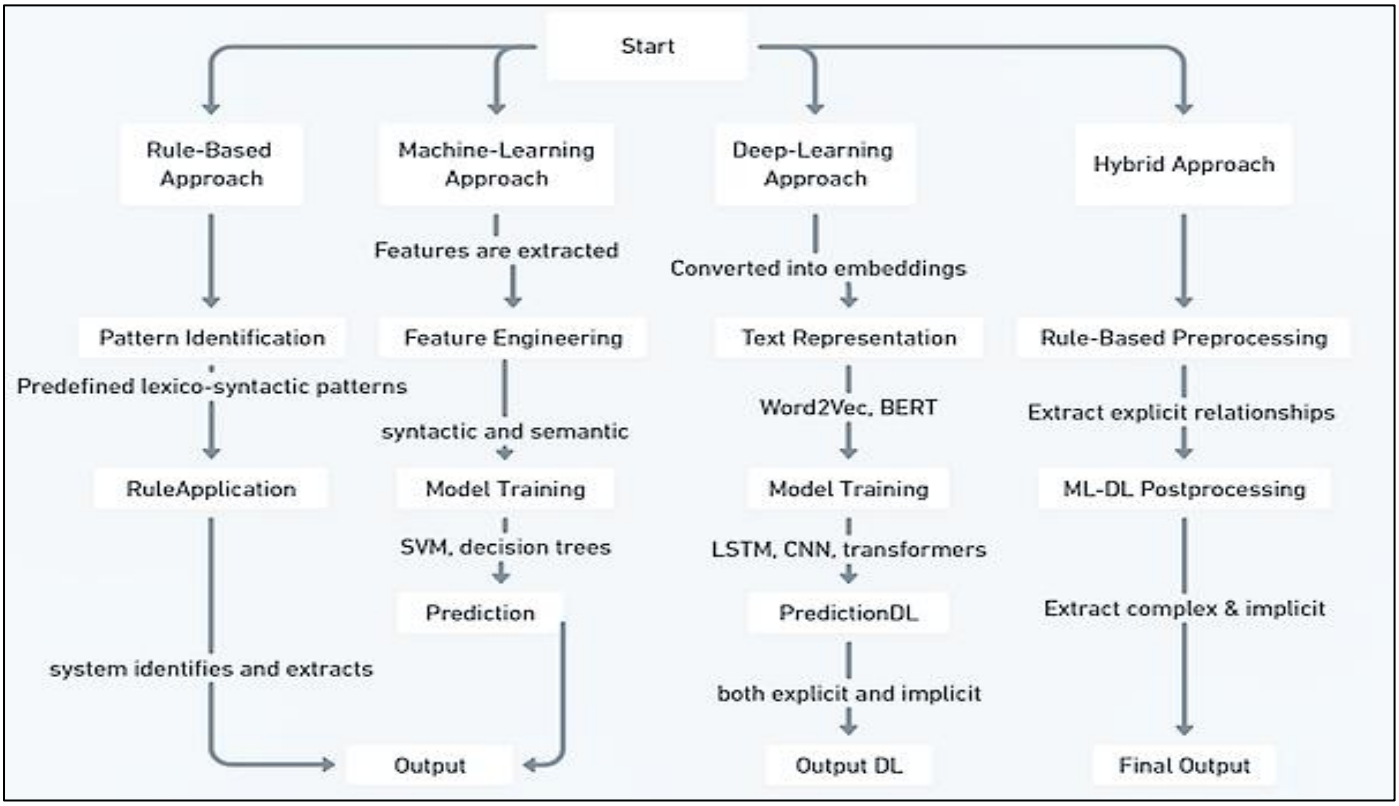

Fig 1 Workflow of Causality Extraction Techniques in Biomedical Literature

The flowchart (Fig-1) visualizes the workflows of different causality extraction techniques, starting from rule-based systems to machine learning, deep learning, and hybrid approaches. It illustrates how each approach processes biomedical text inputs, focusing on pattern identification and predefined rules in rule-based methods, feature extraction and training in machine learning models, and text embedding and automatic learning in deep learning systems. The hybrid approach is highlighted as a combination of rule-based and machine/deep learning methods, offering a comprehensive extraction of both explicit and implicit causal relationships.

Table 5 A Comparison table of Causality Extraction Methods, Detailing Strengths, Weaknesses, and Examples of Models or Tools used.

Technique	Strengths	Weaknesses
Rule-Based Systems	High precision For explicit relationships, easily interpretable	Struggles with implicit relationships, limited scalability
Machine Learning	Flexible, capable of handling different relationship types	Requires manual feature engineering, less effective for complex links
Deep Learning	Automatically learns features, handles implicit relationships	High computational cost, requires large datasets
Hybrid Approaches	Combines the precision of rules and flexibility of ML techniques	Higher system complexity, challenging integration with machine learning models

ISSN No:-2456-2165 https://doi.org/10.5281/zenodo.14603421

The table-5 provides a comparison of four key methods for causality extraction: Rule-Based Systems, Machine Learning, Deep Learning, and Hybrid Approaches. Rule-Based Systems are effective in extracting explicit relationships with high precision but face challenges with implicit relationships and scalability. Machine Learning offers flexibility and handles a variety of relationship types but relies heavily on manual feature engineering, with models such as SVMs and Decision Trees.

Deep Learning, which includes models like LSTM, CNN, and BioBERT, excels in automatically learning features and handling complex, implicit relationships but comes with high computational demands and the need for large datasets. Hybrid Approaches combine the precision of rule-based systems with the flexibility of machine learning, offering improved performance, though they increase system complexity. This comparison is crucial for identifying the most suitable approach on optimizing causality extraction from biomedical literature.

The various techniques used for causality extraction in biomedical text. Rule-based syecision for explicit relationships but are less effective with implicit or complex ones. Machine learning approaches offer flexibility but require substantial feature engineering, while deep learning models automatically learn features from data and handle implicit relationships more effectively.

Hybrid approaches, which combine the strengths of both rule-based and machine learning techniques, offer a balanced solution for more comprehensive causality extraction. These techniques are critical to explore innovative ways to enhance the performance of biomedical causality extraction systems, which will support more robust and accurate analysis of biomedical literature.

V. EVALUATION METRICS

In the context of causality extraction from biomedical text, several key standards are commonly used to assess the effectiveness of individual approaches. These metrics help evaluate the ability of the models to identify true causal relationships while minimizing errors.

A. Common Metrics

The standard evaluation metrics used in causality extraction include Precision, Recall, F1-Score, and Accuracy. These measurements enable a thorough assessment of the frameworks' capability of accurately detect causal relationships while minimizing misclassifications.

- *Precision:*

It measures how many of the identified causal relationships are correctly predicted, ensuring the minimization of false positives.

$$Precision = \frac{True\ Positives}{True\ Positives + False\ Positive} \quad (1)$$

Precision quantifies the ratio of correctly predicted causal relationships to all predicted ones. A high precision score reflects the model's accuracy in identifying causal links while minimizing errors. In biomedical applications, where the stakes of misinformation are high, precision is crucial to ensure that the extracted causal relationships are trustworthy. For instance, precision is essential when identifying causal relationships between drugs and side effects [3], [55].

- *Recall :*

It evaluates the model's capability to detect all true causal relationships, minimizing the risk of false negatives.

$$Recall = \frac{True\ Positives}{True\ Positives + False\ Negatives} \quad (2)$$

Recall quantifies the percentage of actual causal relationships accurately identified by the model, ensuring no true causal relationships are overlooked, which is important in the biomedical field to ensure comprehensive coverage of causal links, such as those related to disease progression and treatment outcomes [56].

- *F1-Score:*

It used for balancing Precision and Recall by taking their harmonic mean, offering a unified measure of a framework's overall robustness in capturing true causal relationships without overemphasizing either precision or recall.

$$F1 - Score = 2 \times \frac{Precision\ \times Recall}{Precision + Recall} \quad (3)$$

The F1-score represents the harmonic mean of precision and recall, offering a balanced evaluation when both metrics are equally significant. In biomedical causality extraction, it is particularly effective for achieving a balance between detecting true causal relationships and minimizing the occurrence of misclassifications or errors [57].

- *Accuracy:*

It simply provides a broader measure of how many predictions the model got correct overall, both causal and non-causal.

$$Accuracy = \frac{True\ Positives + True\ Negatives}{Total\ Predictions} \quad (4)$$

Accuracy calculates the overall percentage of correct predictions, encompassing both true positives and true negatives. However, in imbalanced datasets, common in biomedical research where certain causal relationships are rare, accuracy may fail to fully capture the model's performance, potentially masking deficiencies in identifying minority classes. Thus, it is used in conjunction with other metrics like precision and recall [58]. These metrics are integral to this research, as they offer a quantitative means to evaluate the efficacy of various causality extraction models, providing insights into which approaches work best for biomedical data.

B. Domain-Specific Metrics

In addition to the common metrics, the biomedical domain often requires specific considerations when evaluating causality extraction models:

ISSN No:-2456-2165 https://doi.org/10.5281/zenodo.14603421

➢ *Entity Normalization:*

In biomedical field, entities such as genes, proteins, and diseases must be consistently normalized to ensure accurate representation. This process involves mapping extracted entities to standardized databases like MeSH or UniProt [59], which is ensuring that different mentions of the same entity are correctly unified [35].

➢ *Ambiguity Resolution:*

Biomedical terms are often ambiguous and context-dependent. For example, the same term may refer to different entities or concepts depending on the context in which it appears. Effective causality extraction models must be able to resolve these ambiguities to improve the precision of the extracted relationships, reducing errors caused by misinterpretation of terms [37].

These metrics are vital for ensuring the reliability and robustness of causality extraction models in biomedical texts. Accurate extraction of causal relationships in biomedical literature can have a significant impact on medical research, drug discovery, and patient safety by providing researchers and healthcare professionals with actionable insights. Here is a table summarizing the evaluation metrics used for causality extraction models in biomedical text.

VI. CHALLENGES IN CAUSALITY EXTRACTION FROM BIOMEDICAL TEXT

Causality extraction from biomedical text presents numerous challenges due to the intricacies of the domain and the complexity of the language used. Below are the main challenges that arise in this field.

➢ *Complexity of Biomedical Language*

Biomedical literature is known for its highly technical and complex language, which can pose significant challenges for NLP models. Biomedical texts often contain long, convoluted sentences filled with domain-specific jargon and ambiguous terms. For example, a single term may carry multiple meanings depending on the context (e.g., "cancer" could refer to a disease, a tumor, or even a specific cell line). Moreover, the relationships between biomedical entities, such as genes, proteins, and drugs, are often intricate, multifaceted, and interdependent, further increasing the complexity of accurately extracting and interpreting clear cause-effect relationships. Handling such complexity requires sophisticated models capable of understanding domain-specific nuances, syntactic variations, and implicit causal signals [58], [3].

➢ *Lack of Large Annotated Datasets*

Another key challenge in extracting causality from biomedical texts is the lack of large-scale, annotated datasets. Although there are several biomedical text corpora available, the majority are not annotated for causal relationships, and those that are tend to be small in size. The process of annotating biomedical texts is labor-intensive and requires deep domain expertise, making it difficult to build comprehensive datasets at the scale needed to train effective machine learning and deep learning models.

This scarcity of annotated data limits the development and evaluation of causality extraction models, hindering progress in this area [37], [60]. For instance, datasets such as the BioInfer corpus focus primarily on protein-protein interactions rather than complex causality relations in biomedical studies [35].

➢ *Challenges of Domain Adaptation*

Using general-purpose datasets such as SemEval for biomedical applications presents further complications. While these datasets have been widely used for causality extraction tasks, they are not specifically tailored to the unique features and demands of biomedical text. Domain-specific datasets are crucial because biomedical texts contain distinct structures and relationships not found in other domains.

Therefore, models trained on general purpose datasets often struggle when applied to the biomedical field due to mismatches in linguistic structures, terminologies, and entity relationships. Effective domain adaptation techniques, which adjust models and datasets to biomedical settings, are necessary to overcome this challenge [56], [24].

Therefore, the challenges of causality extraction in the biomedical domain arise from the complexity of the language, the limited availability of annotated datasets, and the need for domain-specific models. Addressing these issues is essential for improving the performance of causality extraction systems in biomedical research, which has the potential to greatly enhance insights in fields like drug discovery, disease treatment, and biological processes.

Table 6 Key Challenges and Solutions in Biomedical Causality Extraction

Key Challenge	Description	Impact on Causality Extraction	Proposed Solution
Language Complexity	Biomedical texts often feature long, complex sentences and ambiguous terminology, making it difficult to identify clear cause-effect relationships.	Extracting causal relationships is complicated by convoluted syntax, medical jargon, and ambiguous terms, leading to missed or incorrect extractions.	It proposed using advanced NLP models (e.g., BioBERT) to better understand context and disambiguate terms, enabling more accurate extraction of complex causal relationships.
Dataset Limitations	The limited availability of large, annotated biomedical datasets for causality extraction presents a significant obstacle to training effective models.	Without sufficient annotated data, machine learning models may not generalize well, leading to	The paper suggests using semi-supervised learning and data augmentation to compensate for the lack of large annotated datasets,

ISSN No:-2456-2165 https://doi.org/10.5281/zenodo.14603421

		poor performance in new contexts.	allowing models to learn more effectively from limited data.
Domain Adaptation	Biomedical texts have unique characteristics that general- purpose datasets (e.g., SemEval) may not fully capture, requiring adaptation for effective use.	Models trained on general-purpose datasets may fail to understand the specific structure and relationships in biomedical literature, reducing their effectiveness.	It introduces domain-specific fine-tuning techniques, where models like BERT are adapted for the biomedical domain using pre-trained biomedical models (e.g., BioBERT), and improving performance on domain-specific tasks.
Implicit Causality	Many causal relationships in biomedical texts are implied rather than explicitly stated, making it difficult for basic ex-traction models to detect them.	Standard models often miss these implicit relationships, leading to an incomplete under- standing of the text's causality.	It explore deep learning models like LSTM and transformers, which are more capable of detecting implicit relationships by understanding broader context and long-range dependencies.
Temporal Dependencies	In biomedical research, the temporal order of events is crucial for understanding causality, but many models overlook this dimension.	Failing to account for temporal relationships can lead to inaccurate causality extraction, particularly in time-sensitive biomedical processes.	It incorporate temporal reasoning into the models, allowing them to recognize the importance of event ordering in extracting meaningful causal links.
Data Imbalance	Biomedical datasets often have an imbalanced distribution of causal and non-causal relationships, skewing model training.	Models may become biased toward overrepresented categories, leading to reduced performance in recognizing underrepresented causal links.	By apply data balancing techniques, such as over-sampling or synthetic data gener-ation, to ensure that models are trained on a more balanced dataset, improving their ability to identify diverse causal patterns.

The key challenges (table-6) in extracting causality from biomedical text include the complexity of language, where long sentences and ambiguous terminology obscure causal links, as well as the limitation of annotated datasets, which hampers model training. Additionally, domain adaptation is crucial, as general-purpose datasets may not fully capture the nuances of biomedical literature, necessitating fine-tuning models like BioBERT for specialized tasks. Implicit causality, where causal relationships are implied rather than explicitly stated, adds another layer of difficulty that deep learning techniques can address.

Temporal dependencies, often overlooked in causality models, are vital in biomedical contexts where the sequence of events affects the interpretation of relationships. Lastly, data imbalance, where non-causal relationships dominate, can bias models, and data balancing techniques are needed to improve model performance.

The paper addresses these challenges by proposing advanced machine learning models, data augmentation, and domain-specific adaptations to enhance causality extraction in biomedical texts.

VII. FUTURE DIRECTIONS

The field of causality extraction from biomedical text continues to evolve, and several promising future directions can significantly enhance the effectiveness of current models and methods.

- *Enhancing Domain-Specific Pre-Trained Models*

While models like BioBERT have made strides in understanding biomedical language, there is still room for improvement. Future efforts should focus on refining these models to better handle the unique complexities of biomedical texts, such as specialized terminology, nuanced sentence structures, and domain-specific knowledge. Incorporating more domain-specific information into the pre-training phase of these models could lead to even greater accuracy in causality extraction [61].

- *Improved Techniques for Implicit Relation Extraction*

One of the biggest challenges in causality extraction is the detection of implicit relationships, where cause and effect are not explicitly stated. Advancing deep learning models, such as those based on transformers [9] and graph neural networks [62], will be key to improving the inference of these implicit relationships. Future research should explore more sophisticated architectures capable of understanding the broader context and underlying semantics of biomedical text, thus enabling the identification of subtle causal links.

- *Expansion of Labeled Datasets*

The limited availability of large, labeled datasets for causality extraction in biomedical texts has been a significant barrier to progress [62]. Expanding these datasets to cover a wider range of biomedical applications, including different subfields of medicine, pharmacology, and genetics, will provide a stronger foundation for training more robust and generalizable models. Furthermore, efforts to create more

ISSN No:-2456-2165 https://doi.org/10.5281/zenodo.14603421

comprehensive and diverse annotated datasets will help models learn better representations and improve their performance across various biomedical tasks [37]. These future directions aim to advance the state-of-the-art in causality extraction from biomedical texts, addressing current limitations and driving innovations that will benefit both the research community and practical applications in healthcare and life sciences.

VIII. CONCLUSION

The extracting causal relationships from biomedical literature is a crucial task that plays a significant role in advancing medical research, drug development, and clinical decision-making. The inherent complexity of biomedical language, characterized by specialized terminology and intricate sentence structures, along with the scarcity of large, annotated datasets, presents formidable challenges to this task. Nevertheless, recent advancements in computational techniques, particularly the use of deep learning models such as LSTMs, CNNs, and transformers like BioBERT, have revolutionized the field by enabling the extraction of both explicit and implicit causal relationships with greater accuracy. Hybrid approaches, which integrate rule-based systems with machine learning and deep learning techniques, have further enhanced performance by leveraging the strengths of each method. This paper makes key contributions by addressing these challenges, providing a detailed comparison of the current methods, and proposing future directions that focus on improving the adaptability and robustness of models specifically tailored for biomedical text. Additionally, the paper emphasizes the importance of expanding labeled datasets to facilitate more effective model training. The research presented here contributes to the ongoing efforts to develop more sophisticated causality extraction systems that can better interpret biomedical literature, ultimately supporting more accurate knowledge discovery in healthcare and life sciences. By overcoming the limitations of existing models and methods, this work lays the foundation for future innovations in biomedical text mining and causal relationship extraction.

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