Analysis of Drug Classification using Mechanism of Action

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Abstract. Mechanism of action (MOA) refers to the specific biochemical interaction through which a drug substance produces its pharmacological effect. A mechanism of action usually includes mention of the specific molecular targets to which the drug binds, such as an enzyme or receptor. Receptor sites have specific affinities for drugs based on the chemical structure of the drug, as well as the specific action that occurs there. Drugs usually work by binding to a receptor and up-regulating (agonist) or down-regulating (antagonist) the production of some downstream cellular activity. If it is known that a disease affects some particular receptor or downstream set of cell activity, then scientists can develop drugs faster if they can predict how cells and genes affect various receptor sites. This paper contains a detailed review on Mechanism of Action.

1. Introduction
The connection of the molecular interactions between the biological target and the therapeutic treatment that produces the physiological response is called as the molecular mechanism of action (MMoA) [1].

It is important to understand the mechanism of action of drugs and some of the reasons as stated below:

It permits the anticipation of problems relating to clinical safety, in the case of anti-infective drug development. Certain drugs are more likely to cause problems of toxicity than those targeting components of the cell wall [2][3].

It can help to recognize those patients who are very likely to respond to a given treatment. Tumors can be screened for the presence of target protein HER2 molecule [4][5].

The target pathway can be monitored in the patient, thereby enabling better dosage. For example, by measuring the patient's blood cholesterol levels, Statin dosage can be determined [4].

The probability of emergence of drug resistance is reduced. By knowing what cellular structure an anti-infective or anticancer drug acts upon, the risk that a single mutation in microbial or tumor DNA will lead to drug resistance and treatment failure can be reduced [2][6][7][8].

It can permit different indications for the identification of the drug [9].

Mechanism of Action of a drug can be determined as follows (figure 1):
Sample of human cells can be treated with the drug and the cellular responses are obtained. Then, the cellular responses are analyzed with algorithms that can search for similarity in already existing genomic databases [10].

![Diagram](image)

**Figure 1. Determination of Mechanism of Action of a drug.**

The remainder of this paper is organized as follows. Section 2 provides a comparative analysis of mechanism of action. Section 3 discusses the data-set and the methodology used. Finally, Section 4 concludes this paper.

2. **Comparative Analysis of Mechanism of Action**

| Reference No. | Findings |
|---------------|----------|
| [11]          | According to the primary mechanism of action of metal-based drugs, they classified metal-based drugs. Based on the currently used metal-based drugs, they provided an analysis of modes of action. |
| [12]          | It described possible solutions to spread knowledge of behaviour interventions changes, and their MoAs. |
| [13]          | Pharmacological activity of Hesp is attributed to the importance of citrus bioflavonoids. Based on mechanism of action of molecules, they described the anti-tumour effects of Hesp in different malignancies. |
| [14]          | Based on cancer model, they covered different genistein interactions with several cellular targets, which will act as a catalyst for the research-based section to apprehend genistein. |
| [15]          | They introduced a tool that can identify kinase inhibitor targets and they described the corresponding mechanism of action of the drug. |
| [16]          | They described the MoA of probiotics and the carcinogens’ and xenobiotics’ inactivation. |
| [17]          | They described the MoA of $^{223}$Ra. This can be used to design different strategies of combination. |
| [18]          | Dissociative designer drugs act as N-methyl-D-aspartate receptor antagonists and |
Persuade adverse outcomes that are alike to the dissociative narcotic ketamine and Phencyclidine.

[19] They showed that Kalirin-7 and Trio Interactomes were revealed by Determinable Proteomics.

[20] The observation is that there exists a positive association between the drug sensitivity and knockout of a drug’s nominal target.

[21] Based on magnitude of MoA profiles, classical mechanism of actions may be sorted. To aid the drug discovery processes, they conducted a study about antibiotic challenge bacterial transcriptome profiles and provided a better approach to help in dereplication of antimicrobial extracts.

[22] They gave various approaches for MoA and identification of targets. They found that several serine proteases were inhibited by bortezomib.

3. Methodology

Figure 2. Machine Learning work-flow.

The work-flow of the machine learning (figure 2) is as follows:
1. Gather the data. Do data pre-processing.
2. Split the data-set into training and testing data-set.
3. Apply various Machine learning models on training data-set.
4. Evaluate the machine learning model on testing data-set.
5. Repeat step 3 and step 4 until the best machine learning model is determined.
6. Deploy the best machine learning model into production.

The data-set is collected through Kaggle website [23]. The data-set provided by Kaggle is already split into testing and training data-set. Furthermore, the training data-set is split into features attributes data-set (Table 2) and target attributes data-set (Table 3). Similarly, the testing data-set is split into features attributes data-set and target attributes data-set.
The training data-set consists of data collected through a cell-based assay designed to capture gene expression and cell viability levels. Based on the patterns in the data, we have to predict a drug’s mechanism of action (MoA). Each of these drugs may have multiple MoA, so this machine learning model is a multilabel classification.

The measurement of gene expression is based on the L1000 assay [24]. The measurement of cell viability is based on the PRISM assay [25]. There are 772 gene expression features, each denoted by "g-". Each gene feature represents the expression of one particular gene. There are 100 cell viability features, each denoted by "c-". Each cell feature represents the viability of one particular cell line.

The description of the features attributes data-set is shown in Table 4. sig_id (Sample ID) is used to uniquely identify each rows in the data-set. cp_type (Treatment/Control) indicates whether the experiment is a treatment (contains drug) or control (contains no drug). cp_type attribute contains two possible values, namely ctl_vehicle and trt_cp. ctl_vehicle indicates that the compound was NOT treated with drug, and it contains only Vehicle Control (e.g. Dimethyl Sulfoxide solvent). trt_cp indicates that the compound was treated with drug. cp_time (Timing) column indicates the treatment duration. cp_dose (Dosage) column indicates the dose level used in the experiment. Generally a higher dose will have a stronger effect.

### Table 2. Sample features attributes of training data-set.

| sig_id     | cp_type  | cp_time | cp_dose | g-0   | g-1   | g-2   | g-3   |
|------------|----------|---------|---------|-------|-------|-------|-------|
| id_0004d9e33 | trt_cp   | 24 D1   |         | -0.5458 | 0.1306 | -0.5135 | 0.4408 |
| id_001897ed | trt_cp   | 72 D1   |         | -0.1829 | 0.232  | 1.208  | -0.4522 |
| id_0034296b | ctl_vehicle | 24 D1   |         | 0.1852  | -0.1404 | -0.3911 | 0.131  |
| id_00276f245 | trt_cp   | 24 D2   |         | 0.4828  | 0.1955 | 0.3825 | 0.4244 |
| id_002791f83 | trt_cp   | 48 D1   |         | -0.3979 | -1.268 | 1.913  | 0.2057 |
| id_004201364 | ctl_vehicle | 24 D1   |         | -0.1561 | -0.2362 | -0.3048 | 1.598  |
| id_006f478b | trt_cp   | 48 D2   |         | 0.3658  | 0.5536 | -0.6898 | -1.627 |
| id_0071665a2 | trt_cp   | 72 D2   |         | 0.0934  | 0.5554 | 1.111  | 0.504  |
| id_007a2159c | trt_cp   | 48 D2   |         | 2.355   | -0.681 | 0.4372 | -0.1076 |
| id_009201382 | trt_cp   | 24 D2   |         | -0.1088 | -0.0244 | 0.8999 | -0.1653 |
| id_00a3939a | trt_cp   | 24 D1   |         | -0.2209 | -0.7875 | 5.572  | 0.1204 |
| id_00c3378b | trt_cp   | 48 D2   |         | -0.4679 | 0.915  | 0.0637 | 0.0247 |
| id_00c8748d | trt_cp   | 24 D1   |         | -0.5296 | -1.145 | -0.5218 | 1.021  |
| id_00d49d16 | trt_cp   | 72 D2   |         | -0.8949 | -0.4096 | -2.695 | 0.4101 |
| id_00e1206f | trt_cp   | 24 D1   |         | -0.0334 | -0.5254 | 0.5886 | -0.5558 |
| id_00f7f922 | trt_cp   | 72 D2   |         | 0.3597  | -0.1423 | -0.1918 | -1.678 |

### Table 3. Sample target attributes of training data-set.

| sig_id  | S-alpha_reductase_inhibitor | 11-beta-hsd1_inhibitor | |
|---------|-----------------------------|-------------------------|
| id_000644bb2 | 1 | 0 | |
| id_000779fc | 0 | 1 | |
| id_00a6266a | 1 | 1 | |
| id_0015df391 | 0 | 1 | |
| id_001626bd3 | 1 | 0 | |
| id_001762a82 | 1 | 1 | |
| id_001bb6df1 | 0 | 0 | |
| id_0020d484 | 0 | 0 | |
| id_00224bf20 | 0 | 0 | |
| id_0023f063e | 0 | 0 | |
| id_002452c7e | 0 | 0 | |
| id_002bcde7o | 0 | 0 | |
4. Conclusion
Mechanism of Action is crucial for the drug discovery process. It can help scientists to create drugs to fight unprecedented diseases. This paper provided a comparative analysis of various research papers. It also contains description of the data-set used for predicting mechanism of action of a drug. In the future, a machine learning model can be developed using the given data-set. The machine learning model can be helpful for the scientists in order to speed up the drug discovery process.

5. References
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Table 4. Description of features attributes of the training data-set.

| No. | Column Name | Description |
|-----|-------------|-------------|
| 1   | sig_id      | Sample ID   |
| 2   | cp_type     | Treatment (contains drug) or Control (contains no drug) |
| 3   | cp_time     | Treatment Duration (24, 48 or 78 hours) |
| 4   | cp_dose     | Dose Level (D1 - Low dose, D2 - High Dose) |
| 5   | g-0, g-1,... g-771 | Gene expression (based on L1000 assay) |
| 6   | c-0, c-1,... c-99 | Cell viability (based on PRISM assay) |
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