**Bliss Interaction Analysis with Bootstrapping**

This repository performs Bliss independence analysis on drug combination screens using optical density (OD) measurements. It supports both a **simple ΔBliss calculation** and a **bootstrapped median-based scoring with interaction bin classification**.

**📁 Expected Input**

**Bliss\_input.txt**

* **Format**: Tab-delimited text file
* **Structure**:
  + **Header row**:
    - First column: (unnamed) Drug A concentrations (in μM or equivalent units)
    - Remaining columns: named as BConc\_ReplicateID (e.g., 1.0\_1, 1.0\_2, 2.5\_1, etc.)
      * BConc should be a float-like value indicating Drug B concentration
  + **Rows**:
    - Each row corresponds to a specific Drug A concentration, with OD values across replicates for various Drug B concentrations.

**Example input file with suffixes indicating replicates:**



**🧮 What the Script Does**

**1. Data Preparation**

* Reads OD measurements from Bliss\_input.txt.
* Extracts and groups OD values by unique concentrations of Drug A and Drug B.

**2. Simple Bliss Independence Model**

* Computes inhibition matrix using:

Inhibition (%)=100×(1−ODControl OD)\text{Inhibition (\%)} = 100 \times \left(1 - \frac{\text{OD}}{\text{Control OD}}\right)Inhibition (%)=100×(1−Control ODOD​)

* Calculates **expected Bliss inhibition** for Drug A and B combination:

EAB=A+B−(A⋅B100)E\_{AB} = A + B - \left(\frac{A \cdot B}{100}\right)EAB​=A+B−(100A⋅B​)

* Outputs a simple ΔBliss matrix:

ΔBliss=ObservedAB−EAB\Delta\_{\text{Bliss}} = \text{Observed}\_{AB} - E\_{AB}ΔBliss​=ObservedAB​−EAB​

**3. Bootstrap-Based ΔBliss Analysis**

* For each combination (excluding zero-dose conditions), performs n\_iterations = 1000 bootstrapped samples.
* For each sample:
  + Resamples single-agent and combo OD values with replacement.
  + Calculates ΔBliss as above.
* Computes **median**, **Q25**, and **Q75** ΔBliss values.
* Assigns an **interaction bin** based on the median ΔBliss value.

| **ΔBliss (Median)** | **Assigned Bin** |
| --- | --- |
| ≥ 10 | Strong synergy |
| 5 to <10 | Moderate synergy |
| 2 to <5 | Weak synergy |
| -2 to <2 | Additive / No interaction |
| -5 to ≤ -2 | Weak antagonism |
| -10 to ≤ -5 | Moderate antagonism |
| < -10 | Strong antagonism |

**4. Visualization**

* **Heatmap** of bootstrapped median ΔBliss values.
* **Bin map** of integer-coded interaction classes using a color scale.

**📤 Output Files**

| **File Name** | **Type** | **Description** |
| --- | --- | --- |
| Simple\_bliss.txt | Tab-delimited .txt | Matrix of simple ΔBliss values per Drug A × Drug B pair |
| bootstrap\_bliss.txt | Tab-delimited .txt | Contains Drug A, Drug B, Median, Q25, Q75, and assigned interaction Bin |
| Delta\_Bliss\_Median\_Heatmap.png | PNG image | Annotated heatmap of median ΔBliss across combinations |
| Delta\_Bliss\_Binmap.png | PNG image | Heatmap of integer-coded bin scores, colored by interaction class |

**📌 Notes**

* **Control OD** is computed as the average OD where **Drug A = 0** and **Drug B = 0**.
* Only combinations where both Drug A and Drug B are non-zero are evaluated.
* Visual outputs use seaborn heatmaps with fixed color palettes for interpretability.

A screenshot of a computer

AI-generated content may be incorrect.Example heatmap outputs

A screenshot of a graph

AI-generated content may be incorrect.