Additional Tables for “DFFNDDS: PREDICTION OF SYNERGISTIC DRUG COMBINATIONS WITH DUAL FEATURE FUSION NETWORKS”

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**Additional tables**

Table S1–S8 contains the ratio of Synergistic/Antagonistic combinations on Drugcomb and DrugcombDB datasets under different splitting settings. Table S9 shows the hyperparamater settings in the compared methods. Table S10 is the results of compared methods with r-drop and without R-drop in DrugcombDB.

Table S1 Ratio of Synergistic/Antagonistic combinations on DrugcombDB under Random splitting setting

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | Cross-validation1 | Cross-validation2 | Cross-validation3 | Cross-validation4 | Cross-validation5 |
| Training set | 24921/60446 | 0.4 | 24827/60540 | 0.4 | 24953/60414 | 0.4 | 24841/60526 | 0.4 | 24960/60407 | 0.4 |
| Validation set | 3116/7555 | 0.4 | 3212/7459 | 0.4 | 3107/7564 | 0.4 | 3163/7508 | 0.4 | 3086/7585 | 0.4 |
| Testing set  | 3128/7543 | 0.4 | 3126/7545 | 0.4 | 3105/7566 | 0.4 | 3161/7510 | 0.4 | 3119/7552 | 0.4 |

Table S2 Ratio of Synergistic/Antagonistic combinations on Drugcomb under Random splitting setting

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | Cross-validation1 | Cross-validation2 | Cross-validation3 | Cross-validation4 | Cross-validation5 |
| Training set | 140622/92982 | 1.5 | 140639/92965 | 1.5 | 140737/92867 | 1.5 | 140634/92970 | 1.5 | 14606/92998 | 1.5 |
| Validation set | 17664/11537 | 1.5 | 17635/11566 | 1.5 | 17639/11562 | 1.5 | 17526/11675 | 1.5 | 17632/11569 | 1.5 |
| Testing set | 17530/11670 | 1.5 | 17542/11658 | 1.5 | 17440/11760 | 1.5 | 17656/11544 | 1.5 | 17578/11622 | 1.5 |

Table S3 Ratio of Synergistic/Antagonistic combinations on Drugcomb under leave one-drug-out splitting setting

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | Cross-validation1 | Cross-validation 2 | Cross-validation 3 | Cross-validation 4 | Cross-validation 5 |
| Training set | 80253/52382 | 1.5  | 86769/58130 | 1.5 | 81094/54312 | 1.5 | 82684/56095 | 1.5 | 78187/52054  | 1.5 |
| Validation set | 26732/17480 | 1.5 | 28929/19371 | 1.5 | 27168/17968 | 1.5 | 27503/18757  | 1.5 | 26166/17248  | 1.5 |
| Testing set  | 8269/5554 | 1.5 | 6286/3393  | 1.9 |  7563/5041 | 1.5 | 7285/4582  | 1.6 | 8947/5966  | 1.5 |

Table S4 Ratio of Synergistic/Antagonistic combinations on Drugcomb under leave-cell line-out splitting setting

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | Cross-validation1 | Cross-validation 2 | Cross-validation 3 | Cross-validation 4 | Cross-validation 5 |
| Training set | 100956/75931 | 1.5 | 110799/72699 | 1.5 | 107912/68726  | 1.5 | 108658/70937 | 1.5 | 111993/75129  | 1.5 |
| Validation set |  36837/25459 | 1.5 | 37066/24100 | 1.5 | 35959/22921 | 1.5 | 36147/23718  | 1.5 | 37319/25055  | 1.5 |
| Testing set  | 28023/14799 | 1.5 | 27951/19390  | 1.5 |  31945/24542 | 1.5 | 31011/21534  | 1.5 | 26504/16005  | 1.5 |

 Table S5 Ratio of Synergistic/Antagonistic combinations on Drugcomb under leave-drugpairs-out splitting setting

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | Cross-validation1 | Cross-validation 2 | Cross-validation 3 | Cross-validation 4 | Cross-validation 5 |
| Training set | 104992/69371 | 1.5  | 105267/69985  | 1.5  | 105069/69158  | 1.5  | 105178/69705  | 1.5  | 106108/70119  | 1.5  |
| Validation set  |  34952/23169  | 1.5 | 35077/23341  | 1.5  | 34981/23095  | 1.5  | 34932/23363  | 1.5  | 35348/23395  | 1.5  |
| Testing set | 35872/23649  | 1.5 | 35472/22863  | 1.5  |  35766/23936 | 1.5  | 35706/23121  | 1.5  | 34360/22675  | 1.5  |

Table S6 Ratio of Synergistic/Antagonistic combinations on DrugcombDB under leave-drugpairs-out splitting setting

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | Cross-validation1 | Cross-validation 2 | Cross-validation 3 | Cross-validation 4 | Cross-validation 5 |
| Training set | 18563/45604  | 0.4 | 18752/45391  | 0.4 | 18672/45555  | 0.4 | 18734/45223  | 0.4 | 18640/45673  | 0.4 |
| Validation set |  6128/15262 |  0.4 |  6232/15149 | 0.4  | 6289/15120  | 0.4 | 6217/15102  | 0.4 |  6274/15164 | 0.4 |
| Testing set |  6474/14678 | 0.4 |  6181/15004 | 0.4 | 6204/14869  | 0.4 | 6214/15219  | 0.4 |  6251/14707 | 0.4 |

Table S7 Ratio of Synergistic/Antagonistic combinations on DrugcombDB under leave-one-drug-out splitting setting

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | Cross-validation1 | Cross-validation 2 | Cross-validation 3 | Cross-validation 4 | Cross-validation5 |
| Training set | 12988/29588  | 0.4 | 16687/44780 | 0.4 | 16140/42787 | 0.4 | 15346/37404  | 0.4 | 16076/40330  | 0.4 |
| Validation set | 4311/9881  | 0.4 | 5525/14965  | 0.4 |  5405/14238 | 0.4 |  5049/12535 | 0.4 |  5288/13515 | 0.4 |
| Testing set | 1910/6148  | 0.3 | 770/940  | 0.8 | 771/1146  | 0.7 | 1085/2539  | 0.4 | 980/1303  | 0.8 |

Table S8 Ratio of Synergistic/Antagonistic combinations on DrugcombDB under leave-cell-line-out setting

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | Cross-validation1 | Cross-validation 2 | Cross-validation 3 | Cross-validation 4 | Cross-validation 5 |
| Training set | 18942/46584  | 0.4 | 17803/42221  | 0.4 | 17908/42385  | 0.4 | 19013/47664  | 0.4 | 18556/46133  | 0.4 |
| Validation set |  6326/15517 |  0.4 |  5853/14156 | 0.4  |  6027/14071 | 0.4 | 6323/15903  | 0.4 | 6175/15388  | 0.4 |
| Testing set  |  5897/13443 | 0.4 |  7509/19167 | 0.4 | 7230/19088  | 0.4 | 5829/11977  | 0.5 | 6434/14023  | 0.5 |

Table S9 Hyperparameter in Compared Models

|  |  |  |  |
| --- | --- | --- | --- |
| Model | Hyperparameter | Values Range | Values |
| DeepSynergy | Drug encoder channels | [32,64,96,128] | 128 |
|  | Context encoder channels | [32,64,96,128] | 128 |
|  | Hidden layer channels | [32,64,96,128] | {128,128,128} |
|  | dropout rate | [0,0.5] | 0.41 |
|  | learning rate | [10-5,10-3] | 5.15e-05 |
| MatchMaker | Drug encoder channels | [32,64,96,128] | {96,96} |
|  | Hidden layer channels | [32,64,96,128] | {96,96} |
|  | drop rate | [0,0.5] | 0.078 |
|  | learning rate | [10-5,10-3] | 0.00031 |
| MRGNN | Drug encoder channels | [32,64,96,128] | 96 |
|  | Hidden layer channels | [32,64,96,128] | 96 |
|  | Drug encoder layers | [2,4,8,16 | 4 |
|  | learning rate | [10-5,10-3] | 0.00058 |
| GCNBMP | Drug encoder channels | [32,64,96,128] | 64 |
|  | Hidden layer channels | [1,2,3,4,5] | 64 |
|  | learning rate | [10-5,10-3] | 0.00079 |
| EPGCNDS | Drug encoder channels | [32,64,96,128] | 128 |
|  | Hidden layer channels | [32,64,96,128] | 96 |
|  | learning rate | [10-5,10-3] | 0.00099 |
| DeepDDS | Context encoder channels | [32,1024],step=256,[32,512],step=128,[32,128],step=32 | [800,160,64] |
|  | Hidden layer channels | [32,64,96,128],[32,64,96,128] | [128,96] |
|  | learning rate | [10-5,10-3] | 0.00063 |
|  | dropout | [0,0.5] |  0.25 |

Table S10 Compared methods With r-drop and Without r-drop in DrugcombDB

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Model | ACC | BACC | Prec | Rec | F1 | ROC-AUC | MCC | KAPPA | AP |
| DFFNDDS | 0.871(0.002) | 0.834(0.002) | 0.801(0.008) | 0.746(0.006) | 0.773(0.003) | 0.921(0.003) | 0.684(0.004) | 0.683(0.004) | 0.859(0.005) |
| DFFNDDS(w.o.rdrop) | 0.866(0.002) | 0.832(0.005) | 0.785(0.010) | 0.750(0.017) | 0.767(0.006) | 0.919(0.003) | 0.673(0.007) | 0.673(0.007) | 0.853(0.007) |
| DeepSynergy | 0.821(0.005) | 0.750(0.009) | 0.758(0.007) | 0.576(0.013) | 0.654(0.017) | 0.750(0.009) | 0.546(0.005) | 0.537(0.006) | 0.561(0.002) |
| DeepSynergy(w.o.rdrop) | 0.827(0.003) | 0.762(0.005) | 0.760(0.010) | 0.604 (0.011) | 0.673 (0.009) | 0.860(0.002) | 0.565 (0.010) | 0.558(0.010) | 0.773(0.008) |
| MatchMaker |

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| 0.820(0.006) |

 | 0.738(0.009) | 0.777(0.013) | 0.542(0.019) | 0.638(0.015) | 0.848(0.008) | 0.538 (0.016) | 0.523 (0.017) | 0.754 (0.014) |
| MatchMaker(w.o.rdrop) | 0.762(0.005) | 0.638(0.009) | 0.698(0.006) | 0.339(0.003) | 0.454(0.002) | 0.746(0.007) | 0.360(0.012) | 0.325(0.005) | 0.568(0.002) |
| MRGNN |

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| --- |
| 0.811(0.003) |

 | 0.745(0.002) | 0.721(0.008) | 0.585(0.005) | 0.646(0.003) | 0.745(0.002) | 0.524(0.006) | 0.519(0.005) | 0.544(0.003) |
| MRGNN(w.o.rdrop) | 0.810(0.003) | 0.737(0.006) | 0.730(0.010) | 0.560 (0.017) | 0.634(0.008) | 0.845(0.001) | 0.517 (0.007) | 0.508(0.008) | 0.734(0.004) |
| GCNBMP | 0.776(0.003) | 0.700(0.014) | 0.652(0.018) | 0.516(0.014) | 0.575(0.002) | 0.700(0.004) | 0.432(0.014) | 0.426 (0.012) | 0.479(0.014) |
| GCNBMP(w.o.rdrop) | 0.802(0.002) | 0.717(0.006) | 0.737(0.014) | 0.511(0.018) | 0.603(0.010) | 0.828(0.005) | 0.492(0.006) | 0.477(0.007) | 0.710(0.007) |
| EPGCNDS |

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| --- | --- | --- | --- | --- |
| 0.751(0.004) |  |  |  |  |

 | 0.645(0.011) | 0.624(0.017) | 0.388(0.040) | 0.477(0.024) | 0.645(0.011) | 0.342(0.009) | 0.325(0.015) | 0.421 (0.008) |
| EPGCNDS(w.o.rdrop) | 0.754(0.003) ) | 0.630(0.013) | 0.672(0.028) | 0.328 (0.039) | 0.438(0.031) | 0.740(0.002) | 0.338(0.012) | 0.305(0.022) | 0.583(0.007) |
| DeepDDS |

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| 0.831(0.002) |

 | 0.748(0.005) | 0.820(0.010) | 0.546(0.012) | 0.655 (0.007) | 0.873(0.001) | 0.569(0.006) | 0 .549(0.008) | 0.779(0.006) |
| DeepDDS(w.o.rdrop) | 0.852(0.002) | 0.784(0.004) | 0.838(0.010) | 0.617(0.011) | 0.711(0.006) | 0.898 (0.002) | 0.628 (0.005) | 0.615(0.006) | 0.826(0.004) |