The definition of Functional Ortholog, Type 2: 1, two genes must have a domain in common; 2, instead of sharing a common GO term, two genes are required to have a GO similarity larger than a pre-defined threshold. Clearly in the following table, if the threshold is too high, functional orthologs will be too limited. On the other hand, if the threshold is with a low value, we will too many orthologs. As such, our recommendation is to set this threshold in the range [0.6, 0.7]. In our experiments, we set it as 0.6.

|  |  |  |  |
| --- | --- | --- | --- |
| Sim threshold | # Yeast Proteins | # Human Proteins | # Ortholog Pairs |
| 0.4 | 2985 | 5853 | 43808 |
| 0.45 | 2797 | 5182 | 33460 |
| 0.5 | 2526 | 4450 | 25213 |
| 0.55 | 2228 | 3723 | 17877 |
| 0.6 | 1909 | 3018 | 13081 |
| 0.65 | 1591 | 2465 | 8542 |
| 0.7 | 1259 | 1596 | 5130 |
| 0.75 | 950 | 1113 | 3429 |
| 0.8 | 700 | 747 | 2163 |
| 0.85 | 506 | 466 | 1222 |
| 0.9 | 423 | 358 | 957 |
| 0.95 | 356 | 274 | 734 |
| 1 | 338 | 251 | 706 |