

Psedo code of Heter-LP

Input

- 1) σ : convergence threshold
- 2) α : diffusion parameter of label propagation
- 3) S_1, S_2, S_3 : homo-subnetwork similarity matrices
- 4) $S_{1,2}, S_{1,3}, S_{2,3}$: hetero-subnetwork matrices
- 5) drugs list (n_1 is the number of total drugs)
- 6) diseases list (n_2 is the number of total diseases)
- 7) targets list (n_3 is the number of total targets)

Output

- 1) F_1, F_2, F_3 : homo-subnetwork matrices of final label values
- 2) $F_{1,2}, F_{1,3}, F_{2,3}$: hetero-subnetwork matrices of final label values

Algorithm

- 1) $F_k=0, F_{k,k'}=0$ for all $k,k'=1,2,3$
- 2) Define three vectors for initial labels: $y_1=0$ with n_1 entries, $y_2=0$ with n_2 entries, $y_3=0$ with n_3 entries

//Projection

- 3) W_1 = projection of $S_{1,2}$ on S_1 ; $size(W_1) = (n_1*n_1)$
- 4) W'_1 = projection of $S_{1,3}$ on S_1 ; $size(W'_1) = (n_1*n_1)$
- 5) W_2 = projection of $S_{1,2}$ on S_2 ; $size(W_2) = (n_2*n_2)$
- 6) W'_2 = projection of $S_{2,3}$ on S_2 ; $size(W'_2) = (n_2*n_2)$
- 7) W_3 = projection of $S_{1,3}$ on S_3 ; $size(W_3) = (n_3*n_3)$
- 8) W'_3 = projection of $S_{2,3}$ on S_3 ; $size(W'_3) = (n_3*n_3)$

//Integration of similarity matrix with projected matrices

9) $M_1 = \text{NormalizeSumOf}(S_1, W_1, W'_1)$

10) $M_2 = \text{NormalizeSumOf}(S_2, W_2, W'_2)$

11) $M_3 = \text{NormalizeSumOf}(S_3, W_3, W'_3)$

// label propagation

12) **for** $i=1..y_1.length$

12.1) $y_1[i]=1, y_1[j]=0$ **for all** $j \neq i$

12.2) $y_2=y_3=0$

12.3) $f_1=y_1, f_2=y_2, f_3=y_3$ // vectors of final label values

12.4) $\text{LabelPropagation}(f_1, f_2, f_3)$

12.5) $\text{Update}(F_1, F_{1,2}, F_{1,3}, i, f_1, f_2, f_3)$

13) **for** $i=1..y_2.length$

13.1) $y_2[i]=1, y_2[j]=0$ **for all** $j \neq i$

13.2) $y_1=y_3=0$

13.3) $f_1=y_1, f_2=y_2, f_3=y_3$

13.4) $\text{LabelPropagation}(f_1, f_2, f_3)$

13.5) $\text{Update}(F_2, F_{2,1}, F_{2,3}, i, f_1, f_2, f_3)$

14) **for** $i=1..y_3.length$

14.1) $y_3[i]=1, y_3[j]=0$ **for all** $j \neq i$

14.2) $y_1=y_2=0$

14.3) $f_1=y_1, f_2=y_2, f_3=y_3$ // vectors of final label values

14.4) $\text{LabelPropagation}(f_1, f_2, f_3)$

14.5) $\text{Update}(F_3, F_{3,1}, F_{3,2}, i, f_1, f_2, f_3)$

15) $F_{1,2} = \text{mean}(F_{1,2}, \text{transpose}(F_{2,1}))$

16) $F_{1,3} = \text{mean}(F_{1,3}, \text{transpose}(F_{3,1}))$

17) $F_{2,3} = \text{mean}(F_{2,3}, \text{transpose}(F_{3,2}))$

18) **return** $F_1, F_2, F_3, F_{1,2}, F_{1,3}, F_{2,3}$

$\text{NormalizeSumOf}(S, W, W')$

1. $d=0$ //a vector with S.numberOfRows length

2. **for** $i=1..S.numberOfRows$

2.1. **for** $j=1..S.numberOfColumns$

2.1.1 **if** ($i \neq j$)

2.1.1.1 $M[i,j]=S[i,j]+W[i,j]+W'[i,j]$

2.1.1.2 $d[i]=d[i]+M[i,j]$

2.1.2 **else** $M[i,j]=0$

2.2 **if** ($d[i]==0$) $d[i]=1$

3. **for** $i=1..M.numberOfRows$

3.1. **for** $j=1..M.numberOfColumns$

3.1.1 **if** ($i \neq j$ and $M[i,j] \neq 0$) $M[i,j] = \frac{M[i,j]}{\sqrt{d[i]d[j]}}$

3. **return** (M)

LabelPropagation(f_1, f_2, f_3)

1. $y_i = f_i$

2. **repeat** (steps 3-12)

//drug

3. $f_{1_old} = f_1$

4. $y'_1 = (I-\alpha)y_1 + \alpha(S_{1,2}*f_2 + S_{1,3}*f_3)$

5. $f_1 = (I-\alpha)y'_1 + \alpha*M_1*f_1$

//disease

6. $f_{2_old} = f_2$

7. $y'_2 = (I-\alpha)y_2 + \alpha((S_{1,2})^T*f_1 + S_{2,3}*f_3)$

8. $f_2 = (I-\alpha)y'_2 + \alpha*M_2*f_2$

//target

9. $f_{3_old} = f_3$

10. $y'_3 = (I-\alpha)y_3 + \alpha((S_{1,3})^T*f_1 + (S_{2,3})^T*f_2)$

11. $f_3 = (I-\alpha)y'_3 + \alpha*M_3*f_3$

12. **while** ($||f_1-f_{1_old}||>\sigma$ *or* $||f_2-f_{2_old}||>\sigma$ *or* $||f_3-f_{3_old}||>\sigma$)

Update ($F_a, F_b, F_c, i, f_1, f_2, f_3$)

1. $F_a[i,]=f_1$
 2. $F_b[i,]=f_2$
 3. $F_c[i,]=f_3$
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