

Article

Generate networks with power-law and exponential-law distributed degrees: with applications in link prediction of tumor pathways

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Abstract

In present study I proposed a method for generating biological networks based on power-law ($p(x)=x^{-\lambda}$) and exponential-law ($p(x)=e^{-\lambda x}$) distribution functions. Given the parameter of power-law or exponential-law distribution function, λ , the algorithm generates an expected frequency distribution according to the given parameter, thereafter creates an adjacency matrix in which (practical) frequency distribution of node degrees matches the expected frequency distribution. The results showed that power-law distribution function performs much better than exponential-law distribution function in generating networks. Using the revised algorithm, tumor related networks (pathways) are simulated and predicted. The results prove that the algorithm is overall effective in predicting network links (14.6%~21.2% of correctly predicted links against 0.1%~3.4% of that for random assignments). Matlab codes of the algorithms are given also.

Keywords power-law; exponential-law; degree distribution; adjacency matrix; network generation; link prediction.

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1 Introduction

In 1999, Barabasi and Albert proposed a well-known mechanism for network evolution. Cancho and Sole (2001) presented an algorithm, which can generate a variety of complex networks with diverse degree distributions. Zhang (2011, 2012a, 2012b, 2012c, 2013, 2015a, 2016a, 2016b), Zhang and Liu (2012) proposed a series of methods and models for network generation and evolution. In present study, I will propose a method for generating biological networks based on power-law and exponential-law distribution functions. Power-law and exponential-law distribution, in particular power-law distribution, is the most popular form of degree distribution of various networks. Therefore, the present method is of significant in the network analysis. Link prediction aims to estimate the likelihood of the existence of a connection between two nodes based on observed connections and the attributes of nodes (Zhang, 2015d; Zhou, 2015). Many biological networks, such as food webs, protein–protein interaction networks and metabolic networks, are incomplete due to missing

links. For example, 80% of the molecular interactions in cells of Yeast (Yu et al., 2008) and 99.7% of human (Amaral, 2008) are still unknown. An incomplete network occurs due to our limited knowledge on a complete network, or the network is in evolution and thus more connections or even nodes are expected with time. Link (connection) prediction can considerably reduce the experimental costs for connection finding, and the algorithms can be used to predict the connections that may appear in the future of evolving networks (Lü and Zhou, 2011; Lü et al., 2012; Zhou, 2015). So far, numerous papers on this topic have been published (Clauset et al., 2008; Guimera and Sales-Pardo, 2009; Barzel and Barabási, 2013; Bastiaens et al., 2015; Lü et al., 2015; Zhang, 2015b, 2015c, 2015d, 2016a, 2016b; Zhang and Li, 2015; Zhao et al., 2015; Zhou, 2015). In present study, I will use the proposed algorithm to approach its effectiveness in link prediction of biological networks.

2 Algorithms

2.1 Generation of the network with power-law or exponential-law distributed degrees

The power-law and exponential-law distribution functions are as follows (Goemann, 2011; Zhang, 2011; Zhang, 2012a; Fig.1)

$$p(x) = x^{-\lambda}$$

$$p(x) = e^{-\lambda x}$$

where λ is a known constant. Suppose there are v nodes in the network being built. First, set the permitted error of degree distribution, er (e.g., 0.05), and the maximum number of simulations, sim (e.g., v^*5), where the fitting error of degree distribution is defined as

$$error = \sum_{i=1}^m |f_i - ff_i| / \sum_{i=1}^m f_i$$

where f_i and ff_i are the expected and practical frequencies of nodes in the degree interval $[in_i, in_{i+1})$ ($i=1,2,\dots, m-1$).

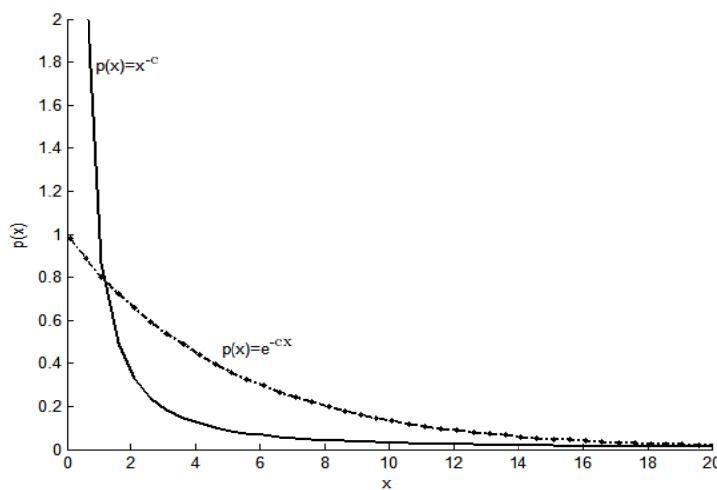


Fig. 1 Illustration of power-law and exponential-law distribution functions.

The algorithm generates an expected frequency distribution according to the given parameter of power-law or exponential-law distribution function, and then creates an adjacency matrix in which (practical) frequency distribution of node degrees coincides with the expected frequency distribution. The adjacency matrix of the network being generated is $d=(d_{ij})$, $i,j=1,2,\dots,v$, where $d_{ij}=d_{ji}$, $d_{ii}=0$, and if $d_{ij}=1$ or $d_{ji}=1$, there is

a connection between nodes i and j . There are $v(v-1)/2$ unknown variables d_{ij} , $i, 1, 2, \dots, v-1; j > i$. However, there are only v known conditions (degrees of v nodes), $s_i, i=1, 2, \dots, v$. Therefore there are in general multiple solutions for $d=(d_{ij})$. I thus use the enumerating/meriting method to find the $d=(d_{ij})$ that meets the error requirement.

The procedures of the algorithm are as the following

- (1) Let $fa=1.2$, and $fac=fa$.
- (2) Find degree intervals $[in_i, in_{i+1})$, $i=1, 2, \dots, m-1$, where

$in_1=1$;
 $in_{i+1}=in_i*fac$, (for power-law distribution)
 $in_{i+1}=in_i*fac^*2$, (for exponential-law distribution)
 $i=1, 2, \dots, m-1$
 $in_m=v$, if $in_m>v$

(3) Let $class=m-1$. Calculate the probability of degree distribution, i.e., the probability of a node's degree falling in the interval $[in_i, in_{i+1})$

$$p_i = in_i^{-\lambda} - in_{i+1}^{-\lambda} \quad (\text{for power-law distribution})$$

$$p_i = e^{-\lambda in_i} - e^{-\lambda in_{i+1}} \quad (\text{for exponential-law distribution})$$

and the corresponding frequencies $f_i=p_i*v$, $i=1, 2, \dots, class-1$. Calculate

$$su = \sum_{i=1}^{class-1} f_i$$

and let $f_{class}=v-su$.

(4) Let initial error, $miner=10^{10}$, and simulation times, $tot=1$.

(5) Let

$$s = \sum_{i=1}^{class} f_i$$

(6) Calculate node degrees

$$s_k = floor(\sum_{i=1}^{class} \sum_{j=1}^{f_i} (in_{i+1} - in_i) * rand + in_i)$$

where $floor(x)$ denotes the integer part of x , $rand$ is a random value in $(0,1)$, $k=1, 2, \dots$

(7) Rearrange v pairs of (node, degree), from greater to smaller in terms of node degrees

v_i, s_i
 v_j, s_j
 \dots
 v_q, s_q

In this step, for each node v_i with s_i expected connections, randomly create v_i-m_i connections to other nodes and each of v_i-m_i nodes has a connection, where m_i is the number of connections already created by

previous nodes.

- (8) Finally, produce the candidate adjacency matrix, $d=(d_{ij})$, calculate the practical frequency distribution, ff_i , $i=1, 2, \dots$, and the *error*.
- (9) If there is at least one node degree, e.g., $s_r=0$, return (6). Otherwise, go to (10).
- (10) If the calculated *error* < *miner*, let *minerr*=*error*, *dd*=*d*, *ffd*_{*i*}=*ff*_{*i*}, go to (11), or else go to (12).
- (11) If *minerr* ≤ *er*, go to (14).
- (12) If *tot* ≥ *sim*, go to (13), or else let *tot*=*tot*+1, return (5).
- (13) Let *fac*=*fac*+0.3, return (2). If *fac*>*v*, go to (14).
- (14) Print adjacency matrix (*dd*), expected and practical frequency distributions (*f*_{*i*} and *ffd*_{*i*}, $i=1, 2, \dots, m$), and node degrees.

The following are Matlab codes of the algorithm (netConstr.m)

```
%Reference: Zhang WJ. 2016. Generate networks with power-law and exponential-law distributed degrees: with applications in
link prediction of tumor pathways. Network Pharmacology, 1(1): 15-35
v=input('Input the number of nodes in the network: ');
typedis=input('Input the type of frequency distribution of degrees (1: Power-law distri (F(x)=1-x^(-c)); 2: Exponential-law
distri (F(x)=1-e^(-cx))): ');
c=input('Input the parametrical value (c) of frequency distribution of node degrees: ');
disp('e.g., c=1.5 for power-law distri (mostly falls in (0, 2]), and c=0.2 for exponential-law distri. For power-law distri, the
following formula can be used to obtain a suitable c, c=1.6347-0.1401m+0.0019v+0.0038m^2, r^2=0.83, p=0.0006<0.01, where
m is the mean of node degrees, v is the number of nodes in the network.')
er=0.05;
sim=v*5;
fa=1.2; % It can be replaced with, e.g., fa=22.6712-34.4086*c+0.0764*v-0.0423*c*v+13.0632*c^2
for fac=fa:0.3:v
in=zeros(1,v);
if (typedis==1)
i=1;
in(1)=1;
while (v>0)
i=i+1;
in(i)=in(i-1)*fac;
if (in(i)>v) in(i)=v; break; end
end; end
if (typedis==2)
i=1;
in(1)=1;
while (v>0)
i=i+1;
in(i)=in(i-1)*fac^2;
if (in(i)>v) in(i)=v; break; end
end; end
deg=in(1:i)
class=i-1;
```

```

ff=zeros(1,class);
p=zeros(1,class);
su=0;
for i=1:class-1
p(i)=netConstrDistr(typedis,c,in(i),in(i+1));
ff(i)=p(i)*v;
su=su+ff(i);
end
ff(class)=v-su;
id=0;
minerr=1e+10;
tot=1;
while (v>0)
[adj0,fff0,error0]=netGen(class,deg,ff);
if (error0<minerr)
adj=adj0; fff=fff0; minerr=error0;
if (minerr<=er) id=1; break; end
end
if (tot>=sim) break; end;
tot=tot+1;
end
if (id==1) break; end
end
fprintf('\nAdjacency matrix of the generated network\n')
disp([adj])
fprintf('\n')
fprintf('\nIntervals of node degrees\n')
for i=1:class
fprintf(['[' num2str(deg(i)) ',' num2str(deg(i+1)) ')  '])
end
fprintf('\n\nExpected frequency distribution of node degrees of the generated network\n')
disp([ff])
fprintf('\n')
fprintf('Practical frequency distribution of node degrees of the generated network\n')
disp([fff])
fprintf(['Fitting error of expected and practical distribution of node degrees of the generated network: ' num2str(minerr) '\n'])
fprintf(['\nNode degrees of the generated network\n' num2str(sum(adj)) '\n'])
fprintf(['\nMean of node degrees of the generated network: ' num2str(mean(sum(adj))) '\n\n\n'])

```

The functions, netConstrDistr.m, and netGen.m, are as follows

```

function pab=netConstrDistr(typedis,lambda,a,b)
pab=0;
if (typedis==1) pab=a^(-lambda)-b^(-lambda); end
if (typedis==2) pab=exp(-lambda*a)-exp(-lambda*b); end

```

```

function [adj,pracff,error]=netGen(m,in,expff)
%pracff[]: degree distri of produced network; er: expected chi-square of practical and expected degree distri
%in[]: degree threshold pairs vector; expff[]: frequency; sim: simulation times
%[in[i],in(i+1)): expff(i), i=1, 2, ..., m; m is the vector dimension
s=sum(expff);
while (m>0)
adj=zeros(s);
pracff=zeros(1,m);
f=zeros(1,s);
p=zeros(1,s);
w=zeros(1,s);
k=0; u=0;
for i=1:m
for j=1:expff(i)
k=k+1;
f(k)=floor((in(i+1)-in(i))*rand()+in(i));
u=u+f(k);
end; end
for i=1:s
p(i)=i;
end
for i=1:s-1
k=i;
for j=i:s-1
if (f(j+1)>f(k)) k=j+1; end
end
l=p(i); p(i)=p(k); p(k)=l;
u=f(i); f(i)=f(k); f(k)=u;
end
for i=1:s
lab=0;
vv=0;
for j=1:i-1
if (adj(j,i)==1)
adj(i,j)=1;
vv=vv+1;
if (vv==f(i)) lab=1; break; end
end; end
if (lab==1) continue; end
cc=0;
for j=1:s
w(j)=j;
end
while (f(i)~=0)

```

```

cs=floor((s-cc)*rand()+1);
if (w(cs)==i) continue; end
if ((adj(w(cs),i)==0) & (w(cs)<i)) continue; end
adj(i,w(cs))=1;
if (cs<s-cc)
for j=cs+1:s-cc
w(j-1)=w(j);
end; end
cc=cc+1;
if (cc>=(f(i)-vv)) break; end
end; end
for i=1:s
for j=1:s
if (adj(j,i)~=adj(i,j)) adj(j,i)=1; adj(i,j)=1; end
end; end
for i=1:s
p(i)=0;
for j=1:s
if (adj(i,j)==1) p(i)=p(i)+1; end
end; end
for i=1:m
pracff(i)=0;
for j=1:s
if ((p(j)>=in(i)) & (p(j)<in(i+1))) pracff(i)=pracff(i)+1; end
end; end
error=sum(abs(expff-pracff))/sum(expff);
isonodes=sum(sum(adj)==0);
if (isonodes==0) break; end
end

```

2.2 Link prediction of the network

Given the adjacency matrix of an original network, i.e., the network with which missing links are prepared for predicting. Suppose the mean of node degrees of the original network is m' . The procedures of the algorithm are as follows

- (1) Let the mean of node degrees of generated network D , $m=m'(1+per)$, where per is the perturbation rate, and $per=0.2, 0.3$, etc., which represents a percentage increment of mean in the network perturbation or evolution.
- (2) Use m to empirically calculate parameter λ (see the section 3.2, eq. (1)).
- (3) Run the algorithm above (section 2.1, with power-law distribution), the resultant adjacency matrix, G , is then achieved.
- (4) Swap rows and columns of G according to the ranking of node degrees of D , such that the same row (column) of G and D has the same ranking of node degree in the respective matrices. By doing so, the final adjacency matrix of the predicted network, H , transformed from G , is achieved.
- (5) Compare H and D , the connection pairs in original network only, connection pairs in predicted (i.e.,

generated) network only, and connection pairs in both original and predicted networks, etc., are thus achieved.

(6) If simulation times are achieved, go to (7); or else return (3).

(7) Calculate means of all indices and mean number (likelihood) of links in original network only, mean number (likelihood) of links in generated network only, and mean number (likelihood) of links in both networks. The percentage of correctly predicted links *vs.* true links is defined as

$$\frac{x}{x+y} \times 100$$

where x is the number of links in both networks, and y is the number of links in original network only. The percentage of correctly predicted links *vs.* predicted links is defined as

$$\frac{x}{x+z} \times 100$$

where x is the number of links in both networks, and z is the number of links in predicted (generated) network only.

The following are Matlab codes of the algorithm (connectionFinding.m). The functions, netConstrDistr.m, and netGen.m, are the same with the above.

```
%Reference: Zhang WJ. 2016. Generate networks with power-law and exponential-law distributed degrees: with applications in link prediction of biological networks. Selforganizology, 6(3):
```

```
clear
```

```
choice=input('Input the type (1 or 2) of data file of the network from which missing links are ready to be predicted (1: adjacency matrix; 2: two array):');
```

```
disp('Adjacency matrix: d=(dij)m*m, where m is the number of nodes in the network. dij=1, if vi and vj are adjacent, and dij=0, if vi and vj are not adjacent; i, j=1,2,..., m');
```

```
disp('Two array: there are two columns, A1 and A2, in the data file; an element of A1 stores a node of a link and the corresponding element of A2 stores another node of the link.');
```

```
if (choice==1)
```

```
adjstr=input('Input the file name of adjacency matrix from which missing links are ready to be predicted (e.g., raw.txt, raw.xls, etc. Adjacency matrix is d=(dij)m*m, where m is the number of nodes in the network. dij=1, if vi and vj are adjacent, and dij=0, if vi and vj are not adjacent; i, j=1,2,..., m: ','s');
```

```
end
```

```
if (choice==2)
```

```
adjstr=input('Input the file name of two array of the network from which missing links are ready to be predicted (e.g., raw.txt, raw.xls, etc. There are two columns, A1 and A2, in the data file; an element of A1 stores a node of a link and the corresponding element of A2 stores another node of the link: ','s');
```

```
end
```

```
pro=input('Input perturbation rate to increase the mean of node degrees of the network (e.g, 0.2, 0.3, etc.):');
```

```
simu=input('Input the simulation times (e.g, 20, 30, etc.):');
```

```
if (choice==1) adjmat=load(adjstr); v=size(adjmat,2); end
```

```
if (choice==2)
```

```
twoarray=load(adjstr);
```

```
nn=size(twoarray,1);
```

```
v=max(max(twoarray));
```

```
for i=1:nn
```

```
adjmat(twoarray(i,1),twoarray(i,2))=1;
```

```

adjmat(twoarray(i,2),twoarray(i,1))=1;
end; end
degr=sum(adjmat);
meanmat=sum(degr)/v;
m=meanmat*(1+pro);
c=1.6347-0.1401*m+0.0019*v+0.0038*m^2;
er=0.05;
sim=v^5;
fa=1.2; %It can be replaced with, e.g., fa=22.6712-34.4086*c+0.0764*v-0.0423*c*v+13.0632*c^2-0.6
percentCorrect=zeros(1,simu);
percentPrediCorrect=zeros(1,simu);
degd=zeros(simu,v);
summ=v*(v-1)/2;
su1=zeros(summ,2*simu);
su2=zeros(summ,2*simu);
su3=zeros(summ,2*simu);
adj=zeros(v);
adjj=zeros(v);
pdegr=zeros(1,v);
pdeg=zeros(1,v);
fdegr=zeros(1,v);
fdeg=zeros(1,v);
fd=zeros(1,v);
pd=zeros(1,v);
persum=zeros(1,3);
for siml=1:simu
for fac=fa:0.3:v
in=zeros(1,v);
i=1;
in(1)=1;
while (v>0)
i=i+1;
in(i)=in(i-1)*fac;
if (in(i)>v) in(i)=v; break; end
end;
deg=in(1:i);
class=i-1;
ff=zeros(1,class);
p=zeros(1,class);
su=0;
for i=1:class-1
p(i)=netConstrDistr(1,c,in(i),in(i+1));
ff(i)=p(i)*v;
su=su+ff(i);
end

```

```

ff(class)=v-su;
id=0;
minerr=1e+10;
tot=1;
while (v>0)
[adj0,fff0,error0]=netGen(class,deg,ff);
if (error0<minerr)
adj=adj0; fff=fff0; minerr=error0;
if (minerr<=er) id=1; break; end
end
if (tot>=sim) break; end;
tot=tot+1;
end
if (id==1) break; end
end
degg=sum(adj);
for h=1:2
if (h==1) fd=degr; end
if (h==2) fd=degg; end
for i=1:v
pd(i)=i;
end
for i=1:v-1
k=i;
for j=i:v-1
if (fd(j+1)>fd(k)) k=j+1; end
end
l=pd(i); pd(i)=pd(k); pd(k)=l;
u=fd(i); fd(i)=fd(k); fd(k)=u;
end
if (h==1) pdegr=pd; fdegr=fd; end
if (h==2) pdeg=pd; fdeg=fd; end
end
for i=1:v
adjj(pdegr(i),:)=adj(pdeg(i),:);
end
for i=1:v
adj(:,pdegr(i))=adjj(:,pdeg(i));
end
degg=sum(adj);
degd(siml,:)=degg;
fprintf('\nAdjacency matrix of the original network\n')
disp([adjmat])
fprintf('\nNode degrees of adjacency matrix of the original network\n')
disp([degr])

```

```

fprintf(['\nMean of node degrees of the original network: ' num2str(mean(degr)) '\n'])
fprintf('\n\nAdjacency matrix of the generated network with power-law distributed node degrees\n')
disp([adj])
fprintf('\nNode degrees of adjacency matrix of the generated network\n')
disp([degg])
fprintf(['\nMean of node degrees of the generated network: ' num2str(mean(degg)) '\n'])
fprintf(['Fitting error of expected and practical distribution of node degrees of the generated network: ' num2str(minerr) '\n\n'])
xx=adjmat & (~adj);
yy=(~adjmat) & adj;
zz=adjmat & adj;
for i=1:3
switch i
    case 1
        mat=xx; s='Connection pairs in original network only (x)';
    case 2
        mat=yy; s='Connection pairs in predicted network only (y)';
    case 3
        mat=zz; s='Connection pairs in both original and predicted networks (z)';
end;
[pairx,pairy]=find(mat);
temp1=pairx; temp2=pairy;
pairxs=pairx(temp1<temp2); pairys=pairy(temp1<temp2);
ConnectionPairs=[pairxs pairys];
persum(i)=size(ConnectionPairs,1);
dm=size(ConnectionPairs,1);
if (i==1) su1(:,siml*2-1)=[pairxs;zeros(summ-dm,1)]; su1(:,siml*2)=[pairys;zeros(summ-dm,1)]; end
if (i==2) su2(:,siml*2-1)=[pairxs;zeros(summ-dm,1)]; su2(:,siml*2)=[pairys;zeros(summ-dm,1)]; end
if (i==3) su3(:,siml*2-1)=[pairxs;zeros(summ-dm,1)]; su3(:,siml*2)=[pairys;zeros(summ-dm,1)]; end
end
percentageCorrect(siml)=persum(3)/(persum(1)+persum(3))*100;
percentagePrediCorrect(siml)=persum(3)/(persum(2)+persum(3))*100;
disp(s)
disp([ConnectionPairs])
disp('Percentages of correctly predicted connections (%): ')
percentageCorrect(siml)
end
disp('-----Summary-----')
disp('Node degrees of original networks: ')
degr=degr
disp('Averaged node degrees of generated networks under different simulations: ')
dega=round(sum(degd)/simu+0.5)
disp('Chi square of node degrees between node degrees of original networks and averaged node degrees of generated networks: ')
chi2=sum(((degr-dega).^2)./degr)
disp('Mean percentage of correctly predicted connections vs. true connections (%): ')
meanPercent=mean(percentageCorrect)

```

```

disp('Standard deviation of mean percentage of correctly predicted connections vs. true connections (%): ')
standardDevi=std(percentageCorrect)
disp('Mean percentage of correctly predicted connections vs. predicted connections (%): ')
meanPercentPredi=mean(percentagePrediCorrect)
disp('Standard deviation of mean percentage of correctly predicted connections vs. predicted connections (%): ')
standardDeviPredi=std(percentagePrediCorrect)
prop1=zeros(v);
prop2=zeros(v);
prop3=zeros(v);
%su2(:,k*2-1),su2(:,k*2)
for i=1:v-1
for j=i+1:v
for k=1:simu
for l=1:v*(v-1)/2
if ((su1(l,k*2-1)==i) & (su1(l,k*2)==j)) prop1(i,j)=prop1(i,j)+1; break; end
if ((su2(l,k*2-1)==i) & (su2(l,k*2)==j)) prop2(i,j)=prop2(i,j)+1; break; end
if ((su3(l,k*2-1)==i) & (su3(l,k*2)==j)) prop3(i,j)=prop3(i,j)+1; break; end
end; end; end
disp('-----')
disp('Mean number (Likelihood) of links in both networks: ')
disp('Node      Node      Likelihood')
[pairx,pairy]=find(prop3);
s=0;
for i=1:v-1
for j=i+1:v
if (prop3(i,j)~=0) s=s+1;pairvalue(s)=prop3(i,j)/simu; end;
end; end
result=[pairx pairy pairvalue'];
ires=sortrows(result,-3);
disp([ires])
clear pairvalue
disp('Mean number (Likelihood) of links in original network only: ')
disp('Node      Node      Likelihood')
[pairx,pairy]=find(prop1);
s=0;
for i=1:v-1
for j=i+1:v
if (prop1(i,j)~=0) s=s+1;pairvalue(s)=prop1(i,j)/simu; end;
end; end
result=[pairx pairy pairvalue'];
ires=sortrows(result,-3);
disp([ires])
clear pairvalue
disp('Mean number (Likelihood) of predicted links in generated network only: ')
disp('Node      Node      Likelihood')

```

```
[pairx,pairy]=find(prop2);
s=0;
for i=1:v-1
for j=i+1:v
if (prop2(i,j)~=0) s=s+1;pairvalue(s)=prop2(i,j)/simu; end;
end; end
result=[pairx pairwise pairvalue'];
ires=sortrows(result,-3);
disp([ires])
```

In link prediction, I use the data of tumor related networks (pathways) (Huang and Zhang, 2012; Li and Zhang, 2013; Pathway Central, 2012). The simulation times are set to be 20. The perturbation rate $per=0$. For comparison, the link prediction with random networks (%) is conducted also.

3 Applications

3.1 Generate networks of power-law/exponential-law distributed node degrees

With different numbers of nodes, v , and distribution parameter, λ , the networks generated by the algorithm are different also (Table 1 and 2). For power-law distribution, the number of degree intervals increases as the parameter λ . The curve of exponential-law distribution function is more flat, thus the number of degree intervals seldom varies (Fig. 1, Table 2).

About the distribution parameter, λ , Goemann et al. (2011) provided a set of values. For power-law distribution, it is 1.63 (transcription network, $v=279$), 1.71 (signaling network, $v=1571$), and 1.58 (metabolic network, $v=1793$), respectively; for exponential-law distribution, it is 0.19 (transcription network), 0.21 (signaling network), and 0.15 (metabolic network), respectively. Zhang (2011) found that for arthropod family networks ($v=66\sim75$), λ values of power-law distribution are 1.64, 1.43, and 1.11, respectively. Based on the investigation on CSM food webs, Zhang and Zhan (2011) found that λ value of exponential-law distribution is between 0.13 and 0.30. Some ecologists found that the mean of node degrees of food webs is around 2.0. Zhang (2011) revealed that the means are 2.16, 4.07, 3.14, 2.84 and 2.19 for the networks of arthropod species respectively. Huang and Zhang (2012) found that the mean is between 2.1 and 2.9 for tumor pathways ($v\approx20\sim100$). Goemann et al. (2011) found that the means are 2.35 (transcription network), 2.18 (signaling network), and 3.09 (metabolic network), respectively. On average the number of connections (links) per species in a food web is roughly 2 (Cohen et al., 1990; Martinez, 1992). However, Shams and Khansari (2014) found that the means are between 4 and 15. Rahman et al. (2013) revealed that the means are between 4.68 and 10.58 for normal and cancer pathways ($v=192\sim631$). Overall power-law λ is mostly around 1.5 (1.5 ± 0.4), and exponential-law λ is around 0.2 (0.2 ± 0.07); the mean of node degrees is mostly around 2.6, and some exceed 4.

In general, λ values and means of node degrees for power-law distribution (Table 1) coincide with the reported findings described above.

Table 1 Generate networks with power-law distributions of node degrees.

Table 1 (continue) Generate networks with power-law distributions of node degrees.

v	200			300		
λ	0.7	1.2	1.7	0.7	1.2	1.7
Intervals	[1,15.3) [15.3,200)	[1,5.1) [5.1,26.01) [26.01,132.651) [132.651,200)	[1,1.5) [1.5,2.25) [2.25,3.375) [3.375,5.0625) [5.0625,7.5938) [7.5938,11.3906) [11.3906,17.0859) [17.0859,25.6289) [25.6289,38.4434) [38.4434,57.665) [57.665,86.4976) [86.4976,129.7463)	[1,18.6) [18.6,300) [26.01,132.651) [132.651,300) [3.375,5.0625) [5.0625,7.5938) [7.5938,11.3906) [11.3906,17.0859) [17.0859,25.6289) [25.6289,38.4434) [38.4434,57.665) [57.665,86.4976) [86.4976,129.7463)	[1,5.1) [5.1,26.01) [26.01,132.651) [132.651,300) [3.375,5.0625) [5.0625,7.5938) [7.5938,11.3906) [11.3906,17.0859) [17.0859,25.6289) [25.6289,38.4434) [38.4434,57.665) [57.665,86.4976) [86.4976,129.7463)	[1,1.5) [1.5,2.25) [2.25,3.375) [3.375,5.0625) [5.0625,7.5938) [7.5938,11.3906) [11.3906,17.0859) [17.0859,25.6289) [25.6289,38.4434) [38.4434,57.665) [57.665,86.4976) [86.4976,129.7463)

														[129.7463,194.6195)	[194.6195,200)	[129.7463,194.6195)	[194.6195,291.9293)	[291.9293,300)									
Expected freq.	170.3690	29.6310	171.6896	99.6136	49.9993	261.2330	38.7670	257.5344	149.4204	74.9989	37.6443	18.8949	9.4840	4.7603	2.3893	1.1993	0.6020	0.3021	0.1517	0.0761	0.0382	0.0192	0.0193				
distri.			24.3030	25.0962	12.5966			36.4545	5.1602			0.8509															
	3.4401	0.5673	6.3226	3.1735																							
			1.5929	0.7995																							
			0.4013	0.2014																							
			0.1011	0.0507																							
			0.0255	0.0257																							
Practical freq.	166	34	168	29	3	99	51	27	255	45	252	43	5	147	78	40	20	8	5	1	1	0	0	0	0		
distri.			0	13	6	3			0																		
			1	0	0																						
			0	0	0																						
			0	0	0																						
Fitting error	0.044		0.047		0.033		0.042		0.044		0.045																
Node degrees	184	178	140	113	55	35	27	25	14	10	9	9	294	261	256	107	91	76	24	14	11	10					
	110	105	104	99	24	23	21	20	7	6	6	6	219	220	209	48	38	25	8	8	8	7					
	97	92	88	85	20	19	19	19	6	6	5	5	209	204	185	24	24	23	7	7	6	6					
	83	79	77	78	16	16	15	15	4	4	4	4	180	173	161	21	20	19	6	5	5	5					
	62	58	41	40	13	12	12	11	3	3	3	3	156	132	123	16	16	17	5	4	4	4					
	38	37	33	32	11	10	8	8	3	3	3	3	117	111	103	17	17	15	4	4	4	4					
	26	21	18	17	7	6	5	5	3	3	3	3	88	86	84	14	14	14	4	4	4	3	3				
	17	14	14	14	5	5	4	4	3	3	3	3	79	78	62	52	14	12	13	3	3	3	3				
	12	14	14	14	4	4	4	4	2	2	2	2	51	53	50	43	13	11	11	3	3	3	3				
	13	14	13	13	4	4	4	4	2	2	2	2	38	36	31	29	9	9	8	7	3	3	3	3			
	14	14	14	14	5	4	4	4	2	2	2	2	29	27	26	26	8	8	7	7	3	3	2	2			
	14	14	14	14	4	4	6	4	2	2	2	2	18	16	18	17	5	6	6	5	2	2	2	2			
	14	13	13	13	4	4	4	4	2	2	2	2	18	17	18	17	5	5	5	5	2	2	2	2			
	16	13	13	13	4	4	4	4	2	2	3	2	18	18	18	17	5	5	6	5	2	2	2	2			
	13	11	12	12	4	4	4	4	2	2	2	1	17	17	17	16	5	5	4	4	2	2	2	2			
	12	12	12	12	4	4	4	4	1	1	1	1	17	17	17	17	4	4	4	4	2	2	2	2			
	11	11	11	11	4	4	5	4	3	1	1	2	17	17	15	16	4	4	4	4	2	2	2	2			
	14	11	12	11	4	4	4	4	2	1	4	1	16	17	16	16	4	4	4	5	2	2	2	2			
	11	13	14	11	4	4	5	5	1	1	1	1	16	16	20	16	4	5	4	4	2	2	2	2			
	10	10	12	11	5	3	3	5	2	1	1	1	16	16	17	16	4	4	4	6	2	2	2	2			
	10	13	15	10	4	3	3	3	1	1	1	2	16	16	15	18	5	4	4	4	2	2	2	2			
	12	10	10	10	3	3	8	2	4	3	1	1	15	15	15	15	4	4	4	4	3	2	2	2			
	10	12	11	9	3	3	3	3	1	1	2	1	15	15	15	15	4	4	4	4	2	2	1	1			
	13	12	13	11	3	3	4	3	1	2	1	1	15	15	14	17	4	4	4	4	2	1	1	2			
	13	10	13	12	3	5	5	5	3	1	1	1	15	15	15	15	5	5	4	4	4	4	1	1			
	11	12	13	12	3	4	4	4	1	1	1	2	16	14	14	14	4	4	4	4	1	1	1	1			
	13	13	12	10	4	4	5	4	1	1	3	1	14	16	19	14	4	4	4	5	1	1	1	1			
	12	9	15	13	3	4	3	2	1	1	1	1	14	14	17	18	5	6	4	4	1	1	1	1			
	13	10	12	13	5	4	5	4	2	2	1	2	14	13	16	14	5	5	4	4	1	1	1	1			
	11	12	12	8	5	3	3	3	1	1	1	1	17	13	13	13	4	4	4	4	1	1	1	1			
	11	11	18	8	5	2	4	3	1	1	3	1	14	17	17	15	4	4	4	4	3	3	1	1			
	13	14	13	11	2	3	2	2	1	1	1	1	13	13	13	13	3	3	4	3	1	1	2	2			
	13	10	12	12	4	2	2	3	1	5	1	1	16	15	15	18	5	5	4	4	1	1	1	1			
	10	12	11	12	3	2	3	2	1	1	1	2	15	12	16	14	3	3	5	4	1	1	1	1			
	11	8	9	11	4	5	2	2	1	2	1	1	12	16	15	12	3	5	3	5	2	1	1	1			
	10	13	13	7	5	2	2	4	1	1	1	1	14	16	16	12	3	3	4	3	1	1	1	1			
	11	7	18	11	2	2	3	3	1	1	1	1	16	12	15	12	3	3	4	3	2	1	1	1			
	9	9	13	9	2	2	4	4	4	1	1	2	16	15	13	15	3	3	3	3	1	1	1	2			
	15	9	12	12	5	2	3	3	1	2	2	1	13	11	18	17	4	3	3	3	3	3	3	1			
	8	13	10	13	3	2	1	4	2	1	3	2	16	17	13	15	3	5	3	3	3	3	3	1			
	10	9	11	15	2	3	2	2	1	2	1	1	12	14	15	15	4	5	3	3	2	2	1	2			
	12	8	13	15	1	6	3	3	1	1	2	1	14	14	14	10	3	3	4	6	1	1	3	1			
	13	9	14	15	1	2	3	6	1	1	1	2	14	13	11	16	3	3	5	5	1	1	3	1			
	12	8	11	10	2	4	3	4	2	1	3	2	13	13	15	13	4	3	3	3	2	1	1	1			
	9	8	15	10	3	3	2	2	1	1	4	1	17	14	18	14	3	3	3	3	2	1	1	3			
	9	7	9	11	3	1	2	3	1	1	1	3	14	16	15	20	2	3	4	5	1	1	2	1			
	12	15	10	9	3	2	4	3	1	1	3	1	16	18	13	17	4	4	2	4	1	1	2	1			
	16	12	14	10	2	2	1	4	1	1	1	1	13	18	15	14	5	4	5	5	1	1	1	1			
	9	11	9	17	4	6	4	8	1	4	2	2	13	18	18	13	4	3	3	4	1	1	2	1			
	9	9	9	12	3	4	5	2	3	4	2	1	14	18	15	16	3	2	3	2	1	1	1	1			
													14	14	14	16	4	2	4	2	3	1	1	2	1		
													15	13	13	15	3	4	4	4	2	1	1	1			
													10	14	18	13	2	3	2	2	1						

	12	16	18	17	4	3	2	3	1	3	1	3
	12	18	13	15	1	3	2	3	1	3	1	6
	12	17	13	17	3	2	2	2	3	1	3	1
	14	14	18	12	2	2	3	3	3	1	1	1
	16	14	8	14	2	5	3	1	3	2	4	2
	13	18	15	14	6	8	1	2	1	6	3	1
	18	9	15	14	11	3	1	2				
	14	18				5	1	3	4			
						4						
Mean of node degrees	20.8		5.4		2.1		27.7		5.8		2.1	

Table 1 (continue) Generate networks with power-law distributions of node degrees.

The adjacency matrix of the network of power-law distribution with $\nu=20$, and $\lambda=1.7$ is

0	1	1	0	0	1	0	0	0	1	0	0	0	1	0	1	1	0	0	1	0
1	0	0	1	1	0	1	0	0	1	0	0	0	0	0	0	0	0	0	0	1
1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0

Table 2 Generate networks with exponential-law distributions of node degrees.

3.2 Relationship between distribution parameter λ , mean of node degrees, number of nodes

For power-law distribution, the following empirical formulae can be used to estimate a suitable λ in using the

algorithm, or estimate the mean of node degrees, which were derived from the results of running the algorithm (Table 1)

$$\lambda = 1.6347 - 0.1401m + 0.0019v + 0.0038m^2, r^2 = 0.83, p = 0.0006 < 0.01 \quad (1)$$

$$m = 36.5867 - 57.9304\lambda + 0.1108\nu - 0.0578\lambda\nu + 22.1056\lambda^2, r^2 = 0.93, p = 0 < 0.01 \quad (2)$$

where m is the mean of node degrees, v is the number of nodes in the network.

3.3 Application in link prediction of tumor related networks (pathways)

Some of the summarized results for link prediction of tumor related network (pathways) are listed in Table 3, in which the mean percentages of correctly predicted connections with random networks (%) are given also.

Compared to the mean percentages of correctly predicted connections *vs.* true connections with random networks, it is obvious that the results of generated networks are effective (Zhou, 2015). Therefore the algorithm is effective in predicting missing links of biological networks.

Table 3 Simulation of some tumor related networks (pathways).

Mean node degrees of generated networks	2	3	2	6	2	2	5	2	4	6	5	2	2	2	2	15	5	3	3	2		
	3	7	2	4	6	7	2	3	4	15	3	2	2	2	8	2	3	3	2			
	21	2	6	2	3	3	3	3	2	2	5	4	3	4	2	2	3	3	2			
	2	2	4	4	3	3	2	2	2	4	8	3	2	2	4	2	3	5				
	3	3	3	3	2	4	2	4	3	3	3	3	3	4	4	2	3	7				
	3	5	2	3	3	8	3	7	2	2	9	3	3	3	2	2	3	3	18			
	3	2	2	4	3	4	3	3	2	4	6	3	18	3	6	2	3	4				
	3	3	2	4	2	2	3	3	7	4	4	4	2	3	4	2	2	8				
	3	2	2	4	4	4	3	5	4	2	2	4	3	8	3	3	2	3				
	3	2	2	2	4	4	17	3	3	3	3	3	3	6	3	4	3	3				
	3	5	2	2	4	3	2	3	3	3	4	4	2	2	3	3	3	3				
	8	2	2	4	6	3	2	3	3	3	3	4	2	5	2	3	2	2				
	2	3	2	4	3	3	2	3	3	2	3	5	3	3	4	4	2	2				
	3	4	2	4	4	3	2	2	2	2	20	2	2		3	2	2	2				
	2	3	3	2	3	4	2	9	2	2	2	2			4	2	2	2				
	2	4	3	3	4	3	2	3	2	8	2	2			7	3	4					
	2	2	2	2	4	3	4	2	6	2	2				4	3						
	3	3	2	2	2	2	2	2	2	4	3	3			2	2						
	3	3	2	2						2	2	3	3			4	2					
	2	4	2	2						4	4	3	3									
	2	3	2	2						2	5	3	2									
	2	2	2	2						2		2	2									
	2	2	2	2						2		2	2									
	8	5	4	2								2	11									
	7	7	2	8																		
	4	15	15	2																		
		2	4																			
		2	2																			
		2	2																			

4 Discussion

For power-law distribution, to reduce the time cost in running the algorithm, the constant, fa , can be approximated with a fitting value (derived from Table 1)

$$fa' = 22.6712 - 34.4086\lambda + 0.0764\nu - 0.0423\lambda\nu + 13.0632\lambda^2, r^2 = 0.93, p = 0 < 0.01 \quad (3)$$

Further, let $fa = fa' - 0.6$. Perturbation rate is a relatively defined parameter. In the practical uses of link prediction, the perturbation rate, per , can be set to be 0.2, 0.5, etc. In addition, the relationship between distribution parameter λ , mean of node degrees, and number of nodes (eq. (1) and (2)) can be further improved, in terms of the specific network issues.

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