Answers to exercises of Chapter 5 (Network Motifs)

1. How were network motifs originally defined in the research literature. What networks are used as null model networks for the detection of statistically significant overrepresented motifs in a real-world network?

Network motifs are originally defined as patterns of local interconnections occurring in complex networks at numbers that are significantly higher than those in randomized networks. A commonly used null hypothesis is based on the frequency distributions of motifs in a sufficiently large ensemble of random networks of appropriate structure, which are used as null model networks. Random networks are considered as null model networks because their structure is generated by a process free of any type of selection acting on their motifs.

2. How do the existing concepts of motif frequency calculation address overlapping matches? Which concept is usually used to specify the frequency of a motif? What is the uniqueness value of a motif?

The three concepts of motif frequency calculation are based on different restrictions on the sharing of network elements for the matches. Frequency concept F1 has no restrictions and considers all matches, even if elements of the target graph have to be used several times. This concept is usually used to specify the frequency of a motif. Concept F2 allows the sharing of vertices but not of edges and therefore calculates the number of instances of a motif that have disjoint edges. For concept F3 matches have to be vertex and edge disjoint and can be seen as nonoverlapping clusters. The frequency calculated by concept F3 is also known as the uniqueness value of a motif.

3. How does a commonly used randomization algorithm work for the generation of the randomized versions of a target network? Which global network property is preserved in these randomized networks?

A commonly applied algorithm in network motif analysis for the generation of randomized versions of a given network arbitrarily rewires the connections of the network locally. Two edges (A,B) and (C,D) are reconnected in such a way that A becomes connected to D and C to B, provided that none of the newly created edges already exist in the network. This algorithm conserves the in and out degree of each vertex and therefore conserves the degree distribution of the network, which is an important property.

4. What are the roles of the vertices of the feed-forward loop motif? How do the three simple duplications of each vertex role look like?

The vertices of the feed-forward loop motif represent three different roles: an input vertex A, an internal vertex B, and an output vertex C. The input vertex A controls the internal vertex B and both jointly control the output vertex C. These vertex roles were termed general regulator (A), specific regulator (B), and target gene (C), respectively, in gene-regulatory networks. The feed-forward loop has three simple generalizations, based on duplicating each of the three roles and their connections. These simple generalizations comprise the following connections (SOURCE_VERTEX,TARGET_VERTEX):
Duplication of the input vertex A:
{(A,B), (A,C), (A',B), (A',C), (B,C)}

Duplication of the internal vertex B:
{(A,B), (A,B'), (A,C), (B,C), (B',C)}
Duplication of the output vertex C:
{(A,B), (A,C), (A,C'), (B,C), (B,C')}

5. Given is the following directed network by a sequence of edges, where each edge is represented by a pair of vertex ID’s (<ID source>, <ID target>): {(1,2), (1,3), (2,3), (2,4), (2,7), (4,5), (4,6), (4,7), (6,5), (8,4), (8,5), (8,10), (9,1), (9,8), (9,10), (10,2), (10,4), (10,1)}. Draw the network and identify all matches of the feed-forward loop motif. Determine the frequency values for each of the three different frequency concepts.

The frequency values for the feed-forward loop motif in the specified network are 9 for frequency concept F1, 5 for concept F2 and 3 for concept F3. The individual matches for the three frequency concepts comprise the following sets of vertices (ordered by the roles of the vertices: input, internal, output):
Frequency concept F1:
{1,2,3}, {2,4,7}, {4,6,5}, {8,10,4}, {9,10,1},
{9,8,10}, {10,1,2}, {10,2,4}, {8,4,5}
Frequency concept F2:
{1,2,3}, {2,4,7}, {4,6,5}, {8,10,4}, {9,10,1}
Frequency concept F3:
{1,2,3}, {4,6,5}, {9,8,10}