Biomockup

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Contents

1 Biomockup

1.1 Introduction

Biomockup is a programming model inspired on biomolecular evolving interactions.

The traditional programming languages allow the explicit definition of the tasks to be performed, down to the smallest detail. The behavior of the programs is deterministic, the same result will always be obtained if the same program is used with the same input data.

This behavior also has practically no tolerance for programming errors: normally, any coding error leads to an alteration of the functionality for which the program has been built, often even a complete suppression of its functionality, through degraded performance in performance or degraded in terms of the operation logic, which is manifested by the correct execution under some sets of input parameters and incorrect in other cases. We will come back to this topic later.

There is therefore a kind of implicit bijection between coding and function. This operating paradigm has proved adequate in a broad spectrum of practical applications. Wherever it has been necessary to implement strategies where it is not desirable to code everything (automatic learning by reinforcement in any of its incarnations, for example), the starting point has always been a traditional programming language, completely bijective.

The observation of the behavior of the logical system which seems to scaffold the life, constituted by networks of interaction between proteins, nucleic acids, ligands and residues of all kinds, inspires us to try another approach based in graph theory.

Our goal is to construct a model of *graphs modifying graphs* that encapsulates some of the logic that we find in molecular biology.

1.2 Proteins: bijection rupture.

The first observation is related to the synthesis of proteins. Their function has a lax dependence on the DNA coding sequence of their original gene, so that in many cases, proteins that only reflect a 30% identity percentage also perform the same function.

The correspondence between the function of the protein and the coding in the gene is rather *suprayective*: the same function is obtained from different initial codings.

The cell achieves this result from the three-dimensional conformation of the protein. The function is not directly expressed in the gene, which is not more than a linear structure (1D), but is achieved by restructuring in space (3D) the amino acid sequence that results from the translation, as if in some way there was a *multidimensional information implicit in the gene*.

This multidimensional information, we know that it is determined by the information 1D, but we also know that the reciprocal is not true: the information of the 3D structure can be related to many linear structures of departure.

A more detailed look to protein folding reveals two logical aspects that we want to emulate:

1) The folding takes place by the generation of new physical interactions: hydrogen bonds, van der waals forces, disulfure bridges,.... So creating new relations between amino acids.

2) This folding generates a *emergence of function* based in the emergence of surface structures that enable the protein to bind to another molecules. This emergence doesn't takes place into the region of internal interaction, but is a consequence of that internal interaction. So, the *logic* of folding operates in a region, and the function appears in other. This is a crucial difference with the programming paradigm of a IT human language: the functionality of an algorithm emerges exactly where the code operates.

NOTE: we are aware that this comparison between life-IT and human-IT is largely naive. It has to be understood as a mere heuristic analogy, without more pretensions.

1.2.1 Interaction model.

Our central idea is to build a linear model of programming blocks (DNA) that undergo a structural transformation to a 2D network. The function will be associated with the appearance of certain motifs within this 2D model. The configuration of this 1D model to 2D will depend on certain predefined interactions between the constituent blocks of our *DNA program*, which we will parameterize in various ways, exploring the possibilities. We will call this parameterization **interaction model (MI)**.

The 2D model will be represented by a graph, which will be generated from structure 1D and MI. We will explore networks with weight between the nodes, the structures based on attractive or repulsive forces and, combined or not with these strategies, the convenience of using hypergraphs and graphs of graphs.

The objective is that the graph is generated automatically from the MI and the linear sequences. The linear sequences are also represented by graphs with nodes connected in a consecutive way.

Well, really the model doesn't speak on dimensions, but on *relations*. A relation between two constituent pieces of DNA (nodes) is represented by an edge of the graph.

The transition from the linear model (regular graph of constant degree 2) is accomplished by the generation of new interactions (creation of new edges between nodes).

An example of interaction model is:

With three types of nodes:

1. N: null generators
2. W: weak generators or short distance generators: generate relation with nodes S,W,N at a distance 3 to 6
3. S: strong generators or long distance generators : generate relation with nodes S at a distance 10 to 15

The computation of the new edges (relations) need be done in a iterative way, because the node distances are modified in every interaction. For instance, the W-generators probably will approach some nodes to the strong generators, otherwise unattainable. It's possible that several models doesn't converge in all the cases.

Note: in this model, we don't take into account, the transcriptional and traslational biological processes, nor their regulation. Our graph DNA is composed yet by amino acid. We only want to emulate the postraslational folding.

1.2.2 Operation model

Or external interaction model. Is the model that makes a protein to bin to another molecule, that enables a graph to bind to another graph. So, it's related with the function.

Once the graph has been obtained from the linear sequence and the MI, it will be necessary to explore this graph in search of structures that are associated with predefined functions. This model that associates reasons with functions is called the operation model (MO).

The search for structures in the network will be implemented by existing specialized software or by our own software if we do not find anything that fits our needs.

How is the operation model defined? The functions that are going to be associated with each motif are going to be somewhat irrelevant for this project. We could simply label them to imply that they are different from each other. However, we will try to make some association with practical meaning in order to illustrate better what we are doing.

But by analogy from life the function is attained by the capability of associate a *protein* with another piece: protein, DNA, . . . , or in our logic abstraction, where all this things are networks,
we need to define an affinity between graphs. In other words, two graphs can bind if both contain some kind of similar subgraphs: k-cores, cliques, . . . We don't now at this moment.

2 Project goals

Explore several implementations of MI and MO and analyze the resulting graphs, in an evolutionary context:

1. Identification of emerging structures.
2. Fault tolerance. Ability of the model to admit random mutations (errors) in the sequence of the initial graph, keeping the previously identified emergent structures.
3. Ease to generate new emerging structures (phase changes?).

Note: this is actually a first piece of an evolution model where fault tolerance allows several versions of the same network to be maintained in a population of graphs, some of them very close to certain phase transitions that would enable the population to generate quickly new functions after changes in environmental restrictions. This evolutionary model could be applied, if we are lucky enough, to the implementation of reinforcement learning strategies and to understand how new functions can emerge surprisingly in highly fault tolerant systems, apparently conservative and thus not prone to functional changes.

3 Example of regular *DNA* graph

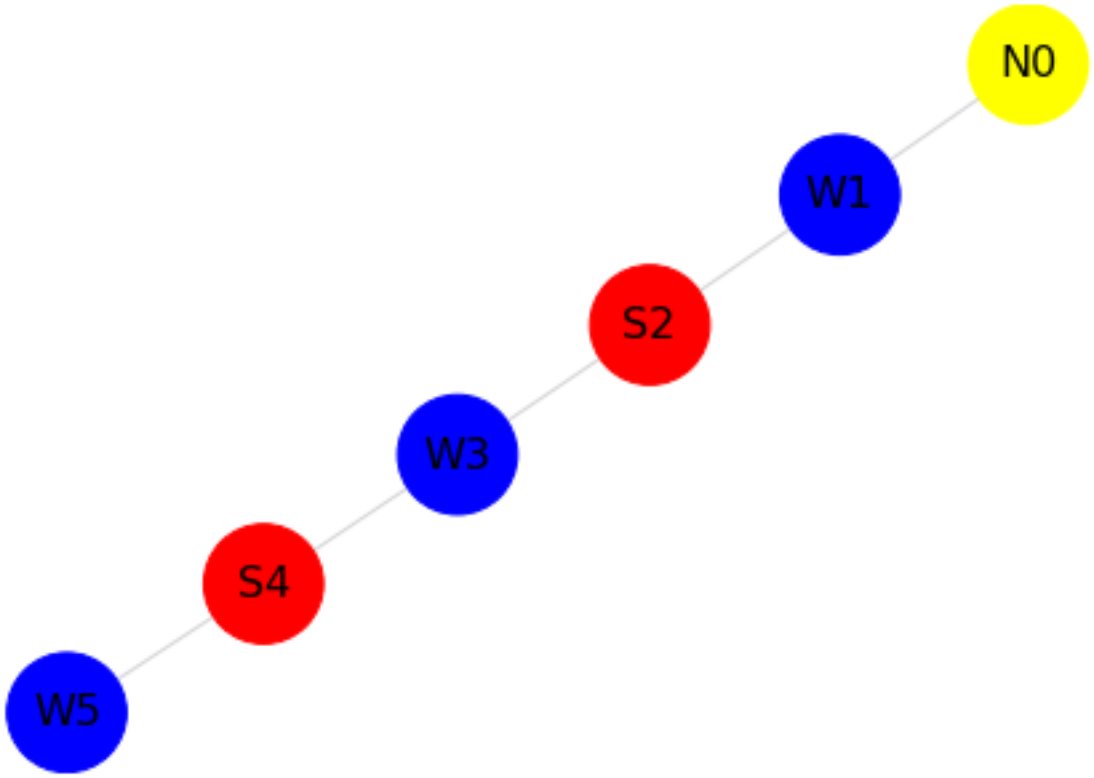
Script 3.0.1 (python)

```python
import warnings
warnings.filterwarnings("ignore")
import networkx as nx
import matplotlib.pyplot as plt
%matplotlib inline
import random
import string
import pandas as pd
# This is a linear regular graph model, the DNA equivalent
G=nx.Graph(name="DNA")
G.add_nodes_from([0,1,2,3,4,5])
G.add_edges_from([(0,1),(1,2),(2,3),(3,4),(4,5)])
labels = {}
labels[0] = 'N0'
labels[1] = 'W1'
labels[2] = 'S2'
labels[3] = 'W3'
labels[4] = 'S4'
labels[5] = 'W5'

colors = []
for label in labels.values():
    if label[0] == "N":
```

```
        colors.append("yellow")
    elif label[0] == "S":
        colors.append("red")
    elif label[0] == "W":
        colors.append("blue")

pos = nx.kamada_kawai_layout(G)
print(colors)
nx.draw(G, pos, with_labels = False, node_color = colors, edge_color = "lightgray",
 ↪  node_size=2000)
nx.draw_networkx_labels(G,pos,labels,font_size = 16);
```

Output

```
['yellow', 'blue', 'red', 'blue', 'red', 'blue']
```



4 Model

4.1 Genoids

Our first entity in our model is the **genoid**, that is the equivalent of a coding gene. The genoid is composed of an arbitrary number of **nucleoids**, as nucleotides are the constituent parts of a gene. The genoid is a ordered

sequence of nucleoids.

The nucleoids could have an arbitrary number of **nucleoid types**, as nucleotides could be adenine, guanine, ...

In our model we simplify the types to a set of cardinality three: **neutral(N)**, **weak(W)** and **strong(S)** interactors.

The genoids are represented by not periodical unidimensional graph meshes. Each node in the graph is a nucleoid.

Each nucleoid is assigned a **nucleoid code**, formed by the concatenation of the nucleoid_type and his sequence number within the genoid.

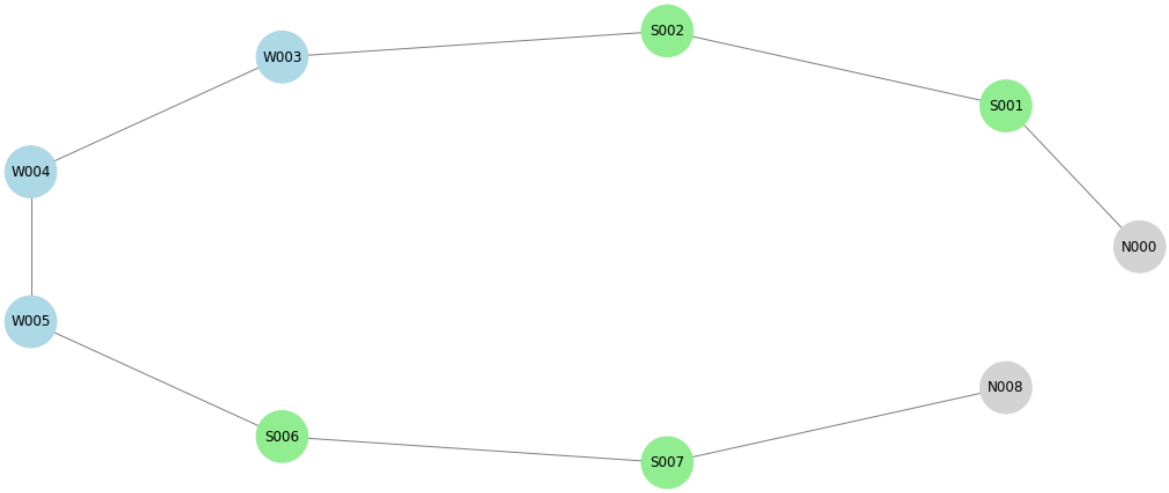
Also a genoid can be represented as a **genoid sequence**, the string formed by the ordered concatenation of nucleoid types.

A **subgenoid** of a given genoid is a genoid formed by a subset of the genoid nucleoids, not necessarily consecutive.

Script 4.1.1 (python)

```python
# Constants

NODE_SIZE_1 = 2000
FONT_SIZE_1 = 12
FIGSIZE_1 = (15, 6)
EDGE_COLOR = "gray"

# Methods
def get_graph_metrics(graph):
    """
    Obtain:
        - The clustering index (C)
        - Average shortest path length (L)
        - Order of the largest connected component (O)
    """
    largest_cc = max(nx.connected_components(graph), key=len)
    largest_connected_subgraph = graph.subgraph(largest_cc)
    if not nx.is_connected(graph):
        subgraph = largest_connected_subgraph
    else:
        subgraph = graph
    return nx.average_clustering(graph),\
           nx.average_shortest_path_length(subgraph),\
           largest_connected_subgraph.order()

def asign_color(nucleoid_type):
    """
    Asign color by nucleoid type
    """
    if nucleoid_type == "N":
        color = "lightgray"
    elif nucleoid_type == "S":
        color = "lightgreen"
    elif nucleoid_type == "W":
        color = "lightblue"
    else:
```

```
        color = "white"
    return color

def genoid_from_sequence(genoid_sequence):
    """
    Create nonperiodic unidimensional grid according to genoid string
    Node string is a sequence of N, W and S
    """
    genoid = nx.Graph(name="DNA")
    i = 0
    nucleoid_codes = {}
    nucleoid_colors = []
    for nucleoid_type in genoid_sequence:
        if i >= 1:
            genoid.add_edges_from([(i-1, i)])
        nucleoid_codes[i] = nucleoid_type + "{:03d}".format(i)
        nucleoid_colors.append(asign_color(nucleoid_type))
        i += 1
    return genoid, nucleoid_codes, nucleoid_colors

def plot_genoid(genoid, nucleoid_codes, nucleoid_colors):
    """
    Plot genoid
    """
    plt.figure(figsize=FIGSIZE_1)
    pos = nx.circular_layout(genoid)
    nx.draw(genoid, pos=nx.circular_layout(genoid), with_labels=False,
            node_color=nucleoid_colors, edge_color=EDGE_COLOR, node_size=NODE_SIZE_1)
    nx.draw_networkx_labels(genoid, pos, nucleoid_codes, font_size=FONT_SIZE_1);

def plot_subgenoid(genoid, subgenoid, genoid_codes, genoid_colors):
    """
    Plot subgenoid
    """
    subgenoid_nodes = subgenoid.nodes()
    subgenoid_codes = {i:genoid_codes[i] for i in subgenoid_nodes}
    subgenoid_colors = [genoid_colors[i] for i in subgenoid_nodes]
    plot_genoid(subgenoid, subgenoid_codes, subgenoid_colors)

genoid, genoid_codes, genoid_colors = genoid_from_sequence("NSSWWWSSN")
plot_genoid(genoid, genoid_codes, genoid_colors)
```



4.2 Proteoids

Script 4.2.1 (python)

```python
# Constants
NODES = "SWN"
def proteoid_from_genoid(genoid, genoid_codes, rule):
    """
    Create relations(edges) into a genoid according to rules, so transforming in a proteoid
    """
    edges_added = {}
    rules = rule.split("|")
    proteoid = genoid.copy()
    for i in range(genoid.order()):
        for generator in rules:
            [nucleoid_type, nucleoid_fin, distance_ini, distance_fin] = generator.split("_")
            distance_ini = int(distance_ini)
            distance_fin = int(distance_fin)
            if genoid_codes[i][0] == nucleoid_type:
                for j in range(i+1, genoid.order()):
                    distance = nx.shortest_path_length(genoid, source=i, target=j)
                    if distance <=distance_fin and distance >= distance_ini and
                     ↪  genoid_codes[j][0] in nucleoid_fin:
                        proteoid.add_edges_from([(i, j)])
                        if nucleoid_type in edges_added:
                            edges_added[nucleoid_type] += 1
                        else:
                            edges_added[nucleoid_type] = 1
    return proteoid, genoid_codes

def generate_proteoid(genoid_sequence, rule, plot=False):
    """
```

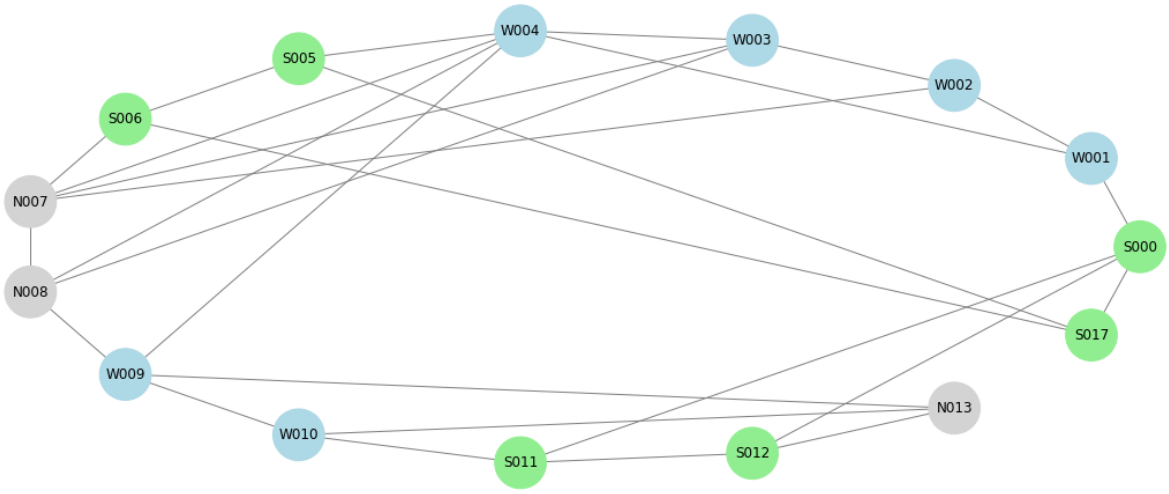
```
    Generate proteoid
    """
    genoid, genoid_codes, proteoid_colors = genoid_from_sequence(genoid_sequence)
    proteoid, proteoid_codes = proteoid_from_genoid(genoid, genoid_codes, rule=rule)
    if plot:
        plot_genoid(proteoid, proteoid_codes, proteoid_colors)
    proteoid_core = nx.k_core(proteoid, k=None, core_number=None)
    proteoid_core_number = nx.core_number(proteoid)
    m = max(proteoid_core_number, key=proteoid_core_number.get)
    proteoid_core_degree = proteoid_core_number[m]
    c, l, o = get_graph_metrics(proteoid_core)
    return c, l, o, proteoid_core, proteoid_core_degree, proteoid, proteoid_codes,
     ↪  proteoid_colors

def random_genoid_sequence(probability_string="NWS", length=20):
    """Generate a random genoid sequence of fixed length and composition"""
    return ''.join(random.choice(probability_string) for i in range(length))

def mutate_genoid_sequence(genoid_sequence, mutations=1, probability_string="NWS"):
    """Generate n mutations in genoid_sequence"""
    genoid_sequence_mutated = list(genoid_sequence)
    for mutation in range(mutations):
        mutation_pos = random.randint(0, len(genoid_sequence) - 1)
        #print("M", mutation_pos, genoid_sequence_mutated)
        probability_string_filtered = ''.join(c for c in probability_string if c !=
         ↪  genoid_sequence_mutated[mutation_pos])
        mutation_char = random.choice(probability_string_filtered)
        #print(mutation_pos, probability_string_filtered,
         ↪  genoid_sequence_mutated[mutation_pos] , "->", mutation_char)
        genoid_sequence_mutated[mutation_pos] = mutation_char
    return ''.join(genoid_sequence_mutated)

def has_tolerance(metric, struct1, struct2, tolerance, verbose=True):
    """
    Retuns if a metric from functional struct1 and functional struct2 are similar
    between a certain tolerance interval
    """
    has_tolerance = True
    if metric in struct1 and metric in struct2:
        m = max(struct1[metric], struct2[metric])
        tolerance = round(int(tolerance)*m/100.0)
        if verbose: print("has_tolerance", struct1[metric], struct2[metric], "Dif:",
         ↪  abs(struct1[metric] - struct2[metric]), "Tolerance", tolerance)
        if abs(struct1[metric] - struct2[metric]) > tolerance:
            has_tolerance = False
            if verbose: print("Tolerance not verified on " + metric + " tolerance " +
             ↪  str(tolerance))
        else:
            if verbose: print("Tolerance verified on " + metric + " tolerance " +
             ↪  str(tolerance))
    elif metric not in struct1 and metric not in struct2:
        has_tolerance = True
```

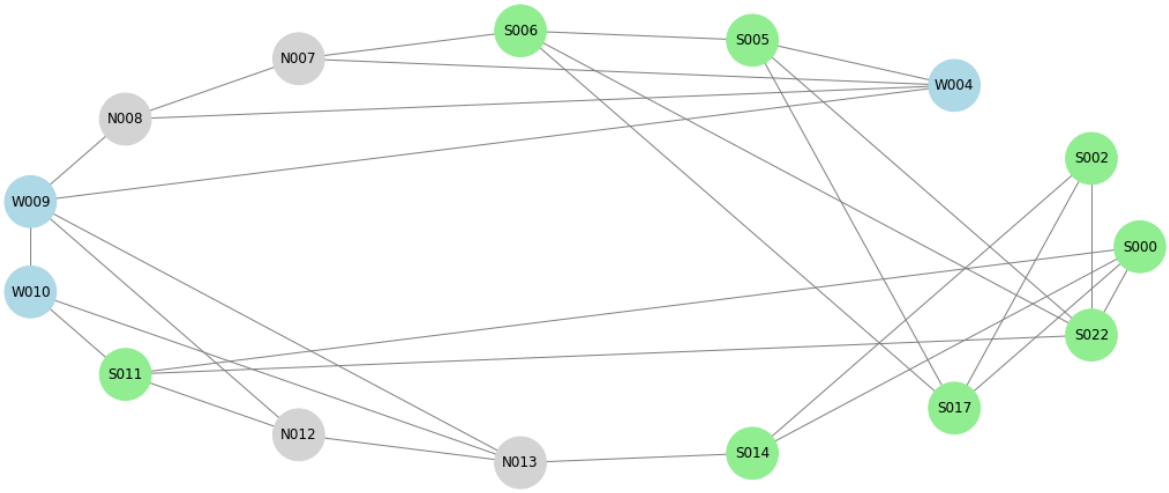
```
        if verbose: print("Tolerance verified on " + metric)
    else:
        has_tolerance = False
        if verbose: print("Tolerance not verified on " + metric)
    return has_tolerance

def get_proteoid_functional_struct(proteoid, proteoid_codes):
    """
    Obtain the functional structure of a proteoid
    """
    proteoid_structure = {}
    nucleoid_types = [proteoid_codes[i][0] for i in proteoid_codes.keys() if i in
    ↪ proteoid.nodes()]
    for nucleoid_type in NODES:
        proteoid_structure[nucleoid_type] = 0
    for nucleoid_type in nucleoid_types:
        proteoid_structure[nucleoid_type] += 1
    proteoid_structure["avg_degree"] = sum(degree for _, degree in
    ↪ proteoid.degree())/proteoid.order()
    proteoid_structure["min_degree"] = min(degree for _, degree in proteoid.degree())
    return proteoid_structure

def compare_proteoid_structs(tolerances, proteoid1, proteoid2, proteoid_codes1,
↪ proteoid_codes2, verbose=True):
    """
    Similarity of genoids by comparing functional structures according to tolerances
    Based on number of nodes W, N, S, the minimun degree and the overall degree with
↪ tolerances
    """
    struct1 = get_proteoid_functional_struct(proteoid1, proteoid_codes1)
    struct2 = get_proteoid_functional_struct(proteoid2, proteoid_codes2)

    for metric in tolerances.keys():
        metric_tolerance = tolerances[metric]
        verify_metric = has_tolerance(metric, struct1, struct2, metric_tolerance, verbose)
        if not verify_metric: return False
    return True


random.seed(20)
genoid_sequence = random_genoid_sequence("NNNNNNNNNNWWWSS", 30)
print(genoid_sequence, len(genoid_sequence))
rule = "W_WN_3_5|S_S_10_30"
c, l, o, proteoid_core, proteoid_core_degree, proteoid, proteoid_codes, proteoid_colors =\
    generate_proteoid(genoid_sequence, rule, plot=False)
plot_subgenoid(proteoid, proteoid_core, proteoid_codes, proteoid_colors)

genoid_sequence_mutated = mutate_genoid_sequence(genoid_sequence, mutations=10,
↪ probability_string="NWS")
print(genoid_sequence_mutated, len(genoid_sequence_mutated))
c, l, o, proteoid_core_mutated, proteoid_core_mutated_degree, proteoid_mutated,
↪ proteoid_codes_mutated, proteoid_colors_mutated =\
```

```
    generate_proteoid(genoid_sequence_mutated, rule, plot=False)
    generate_proteoid(genoid_sequence_mutated, rule, plot=False)
plot_subgenoid(proteoid_mutated, proteoid_core_mutated, proteoid_codes_mutated,
    proteoid_colors_mutated)

struct_proteoid = get_proteoid_functional_struct(proteoid_core, proteoid_codes)
struct_proteoid_mutated = get_proteoid_functional_struct(proteoid_core_mutated,
    proteoid_codes_mutated)
print(struct_proteoid)
print(struct_proteoid_mutated)
tolerances = {'W':10, 'N':20, 'S':10, 'avg_degree':20, 'min_degree':10}
similarity = compare_proteoid_structs(tolerances, proteoid_core, proteoid_core_mutated,
    proteoid_codes, proteoid_codes_mutated, verbose=False)
print("Mutation with fitness consequences:", not similarity)
```

Output

```
SWWWWSSNNWWSSNSNNSNNNNNNNNNNNN 30
SNSNWSSNNWWSNNSNNSNNNNSNNNNNNN 30
{'S': 6, 'W': 6, 'N': 3, 'avg_degree': 3.6, 'min_degree': 3}
{'S': 8, 'W': 3, 'N': 4, 'avg_degree': 3.7333333333333334, 'min_degree': 3}
Mutation with fitness consequences: True
```





5 Mutation cicles

Script 5.0.1 (python)

```python
def plot_graph2(graph, labels, colors, axis, title, title_color):
    """
    Plot graph
    """
    plt.sca(axis)
    axis.set_axis_off()
    pos = nx.circular_layout(graph)
    nx.draw(graph, pos=nx.circular_layout(graph), ax=axis, with_labels = False,
    ↪  node_color=colors, edge_color="gray", node_size=2000)
    nx.draw_networkx_labels(graph, pos, labels, ax=axis, font_size=10)
    plt.title(title, color=title_color, fontsize=9)

def plot_subgraph2(graph, subgraph, graph_labels, graph_colors, axis, title, title_color):
    """
    Plot subgraph
    """
    subgraph_nodes = subgraph.nodes()
    subgraph_labels = {i:graph_labels[i] for i in subgraph_nodes}
    subgraph_colors = [graph_colors[i] for i in subgraph_nodes]
    plot_graph2(subgraph, subgraph_labels, subgraph_colors, axis, title, title_color)

def color_negative_red(val):
    """
    Takes a scalar and returns a string with
    the css property `'color: red'` for negative
    strings, black otherwise.
    """
    color = 'green' if val else 'black'
```

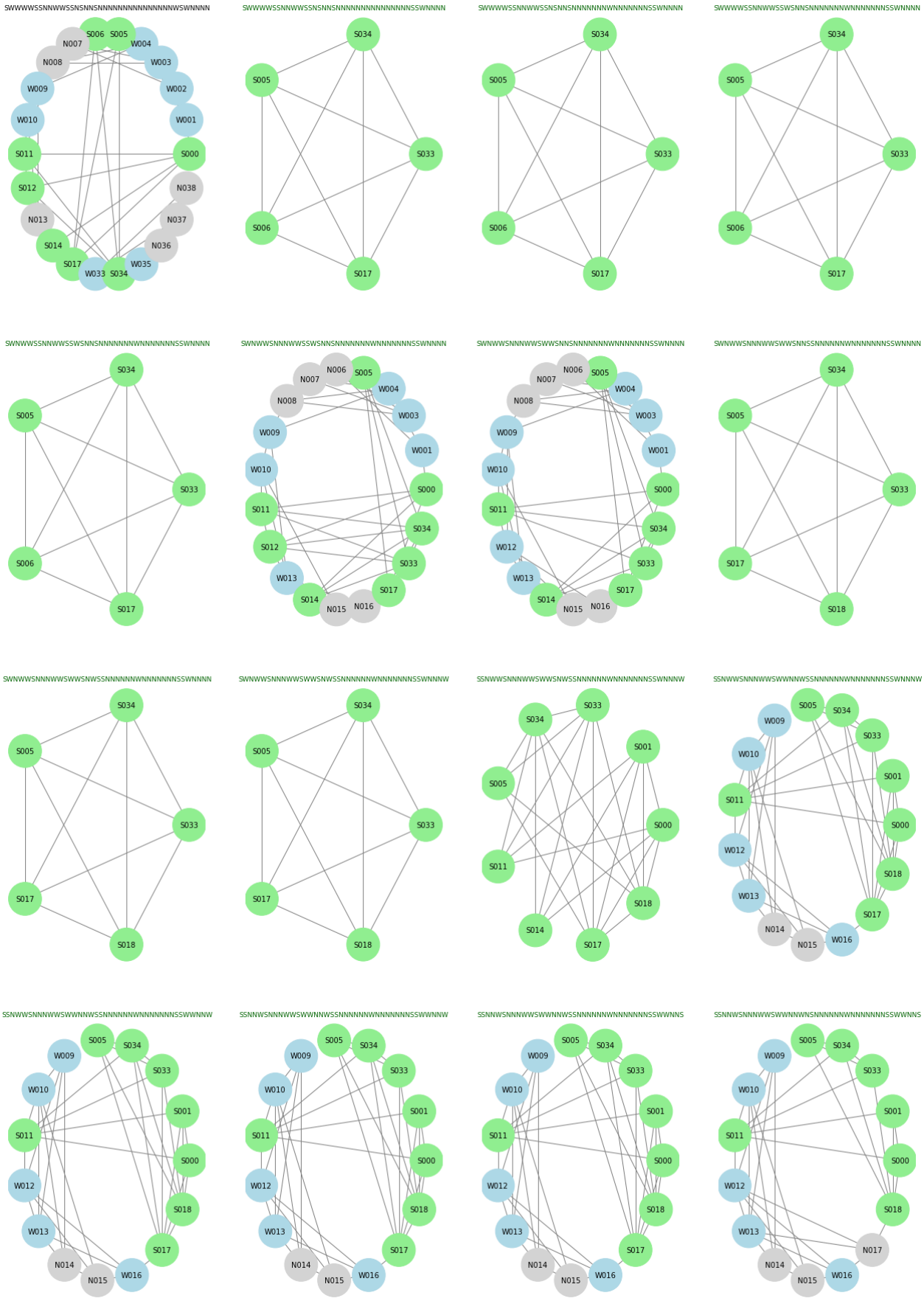
```
    return 'color: %s' % color

def mutation_cicle(graph, c, l, k_core, node_string, labels, colors, tolerances,
↪  mutation_step, mutations_count, probability_string="NWS"):
    """
    """
    assert mutations_count >= 1, "Parameter mutations_count must be greater than 0"
    df = pd.DataFrame(columns=['genoid', 'fitcons','N', 'W', 'S', 'min_degree',
    ↪  'avg_degree', 'order', 'size', 'C', 'L'])
    plot_row = 4
    mutations = {}
    # Add original genoid allele
    mutations_count += 1
    node_string_mutated = node_string
    genoid_orig = get_proteoid_functional_struct(k_core, labels)
    genoid_orig['genoid'] = node_string
    genoid_orig['fitcons'] = False
    genoid_orig['order'] = k_core.order()
    genoid_orig['size'] = k_core.size()
    genoid_orig['C'] = c
    genoid_orig['L'] = l
    df = df.append(genoid_orig, ignore_index=True)
    row_grid = int(mutations_count/plot_row) + 1
    if mutations_count%plot_row == 0: row_grid -= 1
    #print(row_grid)
    plt.axis('off')
    fig, axs = plt.subplots(row_grid, plot_row, figsize=(22, 8*row_grid))
    if row_grid == 1:
        axis = axs[0]
    else:
        axis = axs[0, 0]
    plot_subgraph2(graph, k_core, labels, colors, axis, node_string, "black")
    #print(axs)
    for mutation in range(1, mutations_count):
        node_string_mutated = mutate_genoid_sequence(node_string_mutated,
        ↪  mutations=mutation_step, probability_string=probability_string)
        c, l, o, k_core_mutated, k_core_mutated_degree, graph_mutated, labels_mutated,
        ↪  colors = generate_proteoid(node_string_mutated, rule, plot=False)
        if row_grid == 1:
            axis = axs[mutation]
        else:
            axis = axs[int(mutation/plot_row), int(mutation%plot_row)]
        s_mutated = get_proteoid_functional_struct(k_core_mutated, labels_mutated)
        consequences = not compare_proteoid_structs(tolerances, k_core, k_core_mutated,
        ↪  labels, labels_mutated, verbose=False)
        if consequences: color = "darkgreen"
        else: color = "black"
        plot_subgraph2(graph_mutated, k_core_mutated, labels_mutated, colors, axis,
        ↪  node_string_mutated, color)
        #print(node_string_mutated, "Function", s_mutated, "Consequences", consequences)
        s_mutated['genoid'] = node_string_mutated
        s_mutated['fitcons'] = consequences
```

```
        s_mutated['order'] = k_core_mutated.order()
        s_mutated['size'] = k_core_mutated.size()
        s_mutated['C'] = c
        s_mutated['L'] = l
        df = df.append(s_mutated, ignore_index=True)
    for i in range(int(mutations_count%plot_row), plot_row):
        if row_grid == 1:
            axis = axs[i]
        else:
            axis = axs[row_grid - 1, i]
        axis.set_axis_off()
    print(df)
#     display(df.style.applymap(color_negative_red, subset=['fitcons']).
#             format("{:.2f}", subset=['avg_degree', 'C', 'L']).
#             hide_index().
#             set_properties(**{'text-align': 'left', 'font-family' : 'courier'}))
    plt.show()

random.seed(20)
node_string = random_genoid_sequence("NNNNNNNNNNWWWSS", 40)
rule = "W_WN_3_5|S_S_10_30"
c, l, o, k_core, k_core_degree, graph, labels, colors = generate_proteoid(node_string, rule,
 ↪  plot=False)
#print("C=", c, "L=", l, "O=", o, graph.order(), "k_order_size_degree", k_core.order(),
 ↪  k_core.size(), k_core_degree)
#plot_subgraph(graph, k_core, labels, colors)
tolerances = {'W':20, 'N':50, 'S':10, 'avg_degree':10, 'min_degree':10}
probability_string = "NWS"
mutation_cicle(graph, c, l, k_core, node_string, labels, colors, tolerances,
               mutation_step=1, mutations_count=15, probability_string=probability_string)
```

Output

```
                                    genoid fitcons  N  W  S min_degree  \
0   SWWWWSSNNWWSSNSNNSNNNNNNNNNNNNNNNNWSWNNNN   False  6  8  8          3
1   SWWWWSSNNWWSSNSNNSNNNNNNNNNNNNNNNNSSWNNNN    True  0  0  5          4
2   SWWWWSSNNWWSSNSNNSNNNNNNNWNNNNNNNNSSWNNNN    True  0  0  5          4
3   SWWWWSSNNWWSSWSNNSNNNNNNNWNNNNNNNNSSWNNNN    True  0  0  5          4
4   SWNWWSSNNWWSSWSNNSNNNNNNNWNNNNNNNNSSWNNNN    True  0  0  5          4
5   SWNWWSNNNWWSSWSNNSNNNNNNNWNNNNNNNNSSWNNNN    True  5  6  8          3
6   SWNWWSNNNWWSWWSNNSNNNNNNNWNNNNNNNNSSWNNNN    True  5  7  7          3
7   SWNWWSNNNWWSWWSNNSSNNNNNNWNNNNNNNNSSWNNNN    True  0  0  5          4
8   SWNWWSNNNWWSWWSNWSSNNNNNNWNNNNNNNNSSWNNNN    True  0  0  5          4
9   SWNWWSNNNWWSWWSNWSSNNNNNNWNNNNNNNNSSWNNNW    True  0  0  5          4
10  SSNWWSNNNWWSWWSNWSSNNNNNNWNNNNNNNNSSWNNNW    True  0  0  9          4
11  SSNWWSNNNWWSWWNNWSSNNNNNNWNNNNNNNNSSWNNNW    True  2  5  8          4
12  SSNWWSNNNWWSWWNNWSSNNNNNNWNNNNNNNNSSWWNNW    True  2  5  8          4
13  SSNNWSNNNWWSWWNNWSSNNNNNNWNNNNNNNNSSWWNNW    True  2  5  8          4
14  SSNNWSNNNWWSWWNNWSSNNNNNNWNNNNNNNNSSWWNNS    True  2  5  8          4
15  SSNNWSNNNWWSWWNNWNSNNNNNNWNNNNNNNNSSWWNNS    True  3  5  7          3
```

```
    avg_degree order size         C         L
0     4.000000    22   44  0.329221  2.562771
1     4.000000     5   10  1.000000  1.000000
2     4.000000     5   10  1.000000  1.000000
3     4.000000     5   10  1.000000  1.000000
4     4.000000     5   10  1.000000  1.000000
5     4.526316    19   43  0.292982  2.175439
6     4.526316    19   43  0.305263  2.157895
7     4.000000     5   10  1.000000  1.000000
8     4.000000     5   10  1.000000  1.000000
9     4.000000     5   10  1.000000  1.000000
10    5.111111     9   23  0.548148  1.361111
11    4.800000    15   36  0.539683  1.990476
12    4.800000    15   36  0.539683  1.990476
13    4.800000    15   36  0.539683  1.990476
14    4.800000    15   36  0.539683  1.990476
15    4.400000    15   33  0.540000  2.009524
```


SWWWWSSNNWWSSNSNNSNNNNNNNNNNNNNNWSWNNN
S006
S005
W004
W003
W002
W001
S000
N038
N037
N036
W035
S034
W033
S017
S014
N013
S012
S011
W010
W009
N008
N007
SWWWWSSNNWWSSNSNNSNNNNNNNNNNNNNSSWNNN
S034
S033
S017
S006
S005
SWWWWSSNNWWSSNSNNSNNNNNNNWNNNNNNSSWNNN
S034
S033
S017
S006
S005
SWWWWSSNNWWSSWSNNSNNNNNNNWNNNNNNSSWNNN
S034
S033
S017
S006
S005
SWNWWSSNNWWSSWSNNSNNNNNNNWNNNNNNSSWNNN
S034
S033
S017
S006
S005
SWNWWSNNNWWSWSNNSNNNNNNNWNNNNNNSSWNNN
S034
S033
S017
S014
N015
N016
W013
S012
S011
W010
W009
N008
N007
N006
S005
W004
W003
W001
S000
S034
S033
S017
SWNWWSNNNWWSWSNNSNNNNNNNWNNNNNNSSWNNN
S034
S033
S017
S014
N015
N016
W013
W012
S011
W010
W009
N008
N007
N006
S005
W004
W003
W001
S000
S034
S033
S017
SWNWWSNNNWWSWSNNSNNNNNNNWNNNNNNSSWNNN
S034
S033
S017
S018
SWNWWSNNNWWSWSWSNSSNNNNNNNWNNNNNNSSWNNN
S034
S033
S017
S018
SWNWWSNNNWWSWSNNSNNNNNNNWNNNNNNSSWNNW
S034
S033
S017
S018
SSNWWSNNNWWSWSNNSNNNNNNNWNNNNNNSSWNNW
S033
S034
S001
S005
S000
S011
S018
S014
S017
SSNWWSNNNWWSWWNWSSNNNNNNNWNNNNNNSSWNNW
S005
S034
S033
W009
W010
S001
S011
S000
W012
S018
W013
S017
N014
N015
W016
SSNWWSNNNWWSWSNNSNNNNNNNWNNNNNNSSWNNW
S005
S034
S033
W009
W010
S001
S011
S000
W012
S018
W013
S017
N014
N015
W016
SSNWWSNNNWWSWWNWSSNNNNNNNWNNNNNNSSWWNS
S005
S034
S033
W009
W010
S001
S011
S000
W012
S018
W013
S017
N014
N015
W016
SSNWWSNNNWWSWWNWSSNNNNNNNWNNNNNNSSWWNS
S005
S034
S033
W009
W010
S001
S011
S000
W012
S018
W013
N017
N014
N015
W016

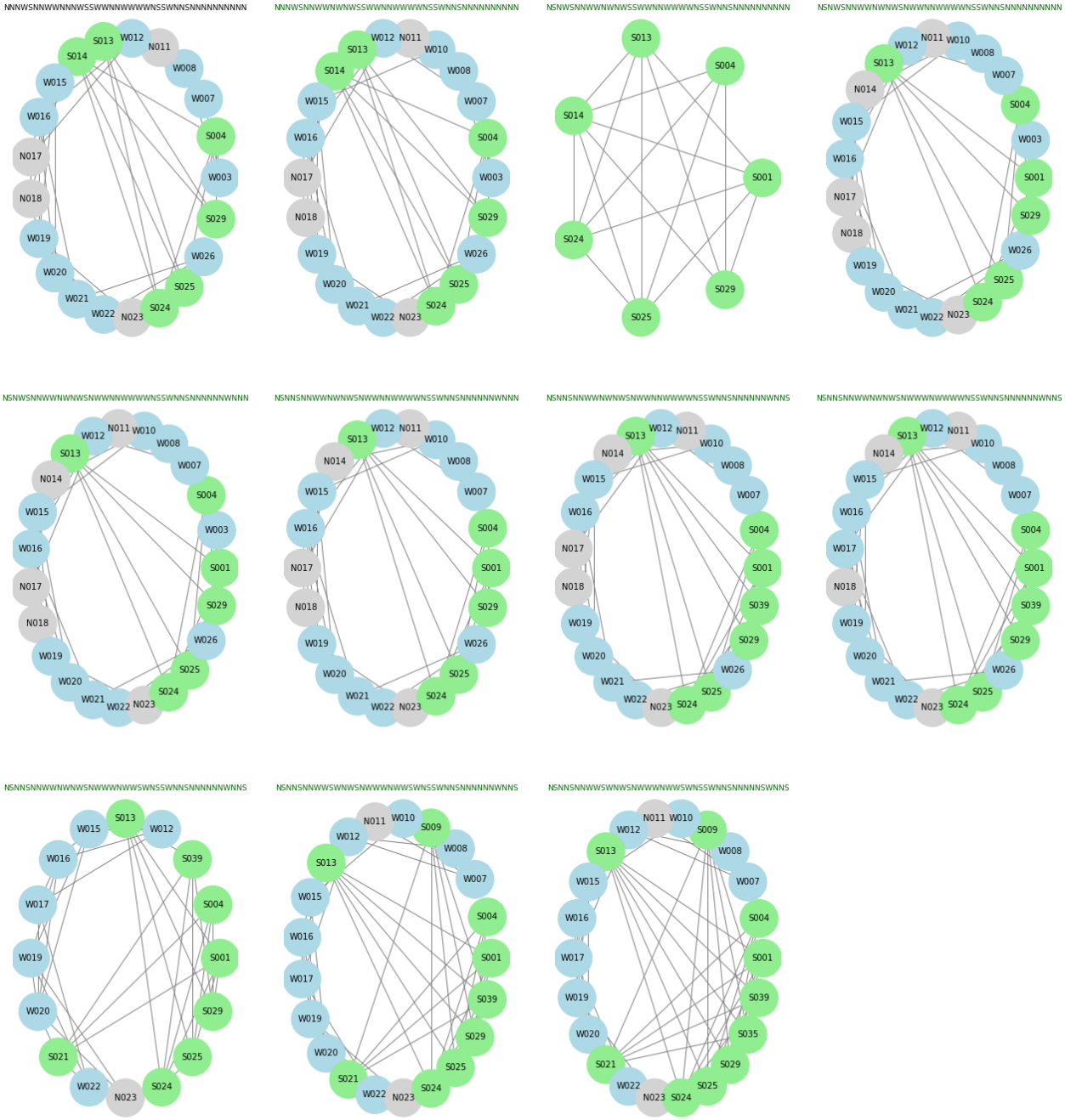
Script 5.0.2 (python)

```python
random.seed(20)
node_string = random_genoid_sequence("NNNNNNNNNNWWWWWSSSS", 40)
rule = "W_WN_3_5|S_S_10_30"
c, l, o, k_core, k_core_degree, graph, labels, colors = generate_proteoid(node_string, rule, plot=False)
#print("C=", c, "L=", l, "O=", o, graph.order(), "k_order_size_degree", k_core.order(), k_core.size(), k_core_degree)
#plot_subgraph(graph, k_core, labels, colors)
tolerances = {'W':20, 'N':50, 'S':10, 'avg_degree':10, 'min_degree':10}
probability_string = "NWS"
mutation_cicle(graph, c, l, k_core, node_string, labels, colors, tolerances,
               mutation_step=1, mutations_count=10, probability_string=probability_string)
```

Output

	genoid	fitcons	N	W	S	min_degree	\
0	NNNWSNNWWNNNWSSWWNNWWWWNSSWNNSNNNNNNNNNN	False	4	11	6	3	
1	NNNWSNNWWNWNWSSWWNNWWWWNSSWNNSNNNNNNNNNN	True	4	12	6	3	
2	NSNWSNNWWNWNWSSWWNNWWWWNSSWNNSNNNNNNNNNN	True	0	0	7	4	
3	NSNWSNNWWNWNWSNWWNNWWWWNSSWNNSNNNNNNNNNN	True	5	12	6	3	
4	NSNWSNNWWNWNWSNWWNNWWWWNSSWNNSNNNNNNWNNN	True	5	12	6	3	
5	NSNNSNNWWNWNWSNWWNNWWWWNSSWNNSNNNNNNWNNN	True	5	11	6	3	
6	NSNNSNNWWNWNWSNWWNNWWWWNSSWNNSNNNNNNWNNS	True	5	11	7	3	
7	NSNNSNNWWNWNWSNWWWNWWWWNSSWNNSNNNNNNWNNS	True	4	12	7	3	
8	NSNNSNNWWNWNWSNWWWNWWSWNSSWNNSNNNNNNWNNS	True	1	7	8	4	
9	NSNNSNNWWSWNWSNWWWNWWSWNSSWNNSNNNNNNWNNS	True	2	10	9	4	
10	NSNNSNNWWSWNWSNWWWNWWSWNSSWNNSNNNNNSWNNS	True	2	10	10	4	

	avg_degree	order	size	C	L
0	4.476190	21	47	0.451020	2.276190
1	4.545455	22	50	0.418615	2.285714
2	4.857143	7	17	0.752381	1.190476
3	4.434783	23	51	0.386542	2.359684
4	4.434783	23	51	0.386542	2.359684
5	4.363636	22	48	0.419264	2.354978
6	4.521739	23	52	0.432919	2.359684
7	4.782609	23	55	0.443064	2.316206
8	4.750000	16	38	0.377083	1.975000
9	5.142857	21	54	0.380499	2.104762
10	5.363636	22	59	0.392316	2.099567


NNNWSNNWWNNNWSSWWNNWWWWWNSSWNNSNNNNNNNNNN
S013 W012 N011 S014 W008 W015 W007 W016 S004 N017 W003 N018 S029 W019 W026 W020 S025 W021 W022 N023 S024
NNNWSNNWWNWNWSSWWNNWWWWNSSWNNSNNNNNNNNNN
S013 W012 N011 W010 S014 W008 W015 W007 W016 S004 N017 W003 N018 S029 W019 W026 W020 S025 W021 W022 N023 S024
NSNWSNNWWNWNWSSWWNNWWWWNSSWNNSNNNNNNNNNN
S013 S004 S014 S001 S024 S029 S025
NSNWSNNWWNWNWSNWWNNWWWWNSSWNNSNNNNNNNNNN
N011 W012 W010 W008 S013 N014 W007 S004 W015 W003 W016 S001 N017 S029 N018 W026 W019 S025 W020 S024 W021 W022 N023
NSNWSNNWWNWNWSNWWNNWWWWNSSWNNSNNNNNNWNNN
N011 W012 W010 W008 S013 N014 W007 S004 W015 W003 W016 S001 N017 S029 N018 W026 W019 S025 W020 S024 W021 W022 N023
NSNNSNNWWNWNWSNWWNNWWWWNSSWNNSNNNNNNWNNN
N011 W012 W010 W008 S013 N014 W007 S004 W015 W016 S001 N017 S029 N018 W026 W019 S025 W020 S024 W021 W022 N023
NSNNSNNWWNWNWSNWWNNWWWWNSSWNNSNNNNNNWNNS
N011 W012 W010 W008 S013 N014 W007 W015 S004 W016 S001 N017 S039 N018 S029 W019 W026 W020 S025 W021 W022 N023 S024
NSNNSNNWWNWNWSNWWNNWWWWNSSWNNSNNNNNNWNNS
N011 W012 W010 W008 S013 N014 W007 W015 S004 W016 S001 N017 S039 N018 S029 W019 W026 W020 S025 W021 W022 N023 S024
NSNNSNNWWNWNWSNWWNNWWWWSWNSSWNNSNNNNNNWNS
S013 W015 W012 W016 S039 W017 S004 W019 S001 W020 S029 S021 S025 W022 N023 S024
NSNNSNNWWSWNWSNWWNNWWWWSWNSSWNNSNNNNNNWNNS
N011 W010 S009 W012 W008 S013 W007 W015 S004 W016 S001 W017 S039 W019 S029 W020 S025 S021 W022 N023 S024
NSNNSNNWWSWNWSNWWNNWWWWSWNSSWNNSNNNNNSWNNS
N011 W010 W012 S009 W008 S013 W007 W015 S004 W016 S001 W017 S039 W019 S035 W020 S029 S021 S025 W022 N023 S024