

Supplementary material

GeoFold: Topology-based protein unfolding pathways capture the effects of engineered disulfides on kinetic stability.

Vibin Ramakrishnan^{1,2,5}, Sai Praveen Srinivasan^{1,4}, Saeed M Salem^{3,7}, Suzanne J Matthews^{3,6}, Wilfredo Colón^{1,4}, Mohammed Zaki³, Christopher Bystroff^{1,2,3*},

Contents:

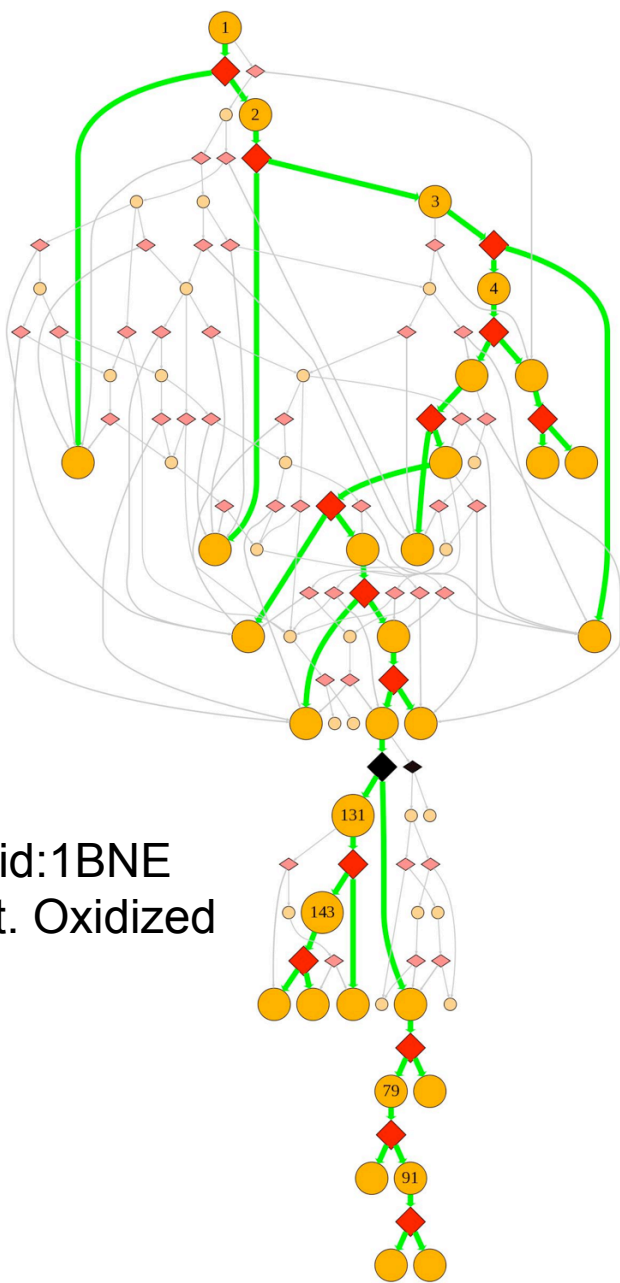
p 2.....	Guide to Geofold DAGs
p 3.....	Geofold DAG for PDBid:1BNE Barnase 43-80 mutant. Oxidized $\omega=40$
p 4.....	Geofold DAG for PDBid:1BNF Barnase 70-92 mutant. Oxidized $\omega=40$
p 5.....	Geofold DAG for PDBid:1BNG Barnase 95-102 mutant. Oxidized $\omega=40$
p 6.....	Geofold DAG for PDBid:1L35(modified) Lysozyme 3-97 mutant. Oxidized. $\omega=40$
p 7.....	Geofold DAG for PDBid:1L35(modified) Lysozyme 9-164 mutant. Oxidized. $\omega=40$
p 8.....	Geofold DAG for PDBid:1L35(modified) Lysozyme 21-142 mutant. Oxidized. $\omega=40$
p 9.....	Geofold DAG for PDBid:1L35(modified) Lysozyme 90-122 mutant. Oxidized. $\omega=40$
p 10.....	Geofold DAG for PDBid:1L35(modified) Lysozyme 127-154 mutant. Oxidized. $\omega=40$
p 11-14.....	Geofold DAG for PDBid:1LYD wild-type Lysozyme $\omega=10, 20, 30, 40$
p 15-17.....	Geofold DAG for PDBid:7DFR wild-type $\omega=10, 40, 60$
p 18.....	Geofold DAG for PDBid:7DFR(modified) P39C mutant. $\omega=15$
p 19.....	Geofold DAG for PDBid:3jrh wild type FIS $\omega=40$
p 20.....	Geofold DAG for PDBid:3jrh (modified) FIS S30C mutant $\omega=40$
p 21.....	Geofold DAG for PDBid:3jrh (modified) FIS V58C mutant $\omega=40$

Guide to GeoFold DAGs

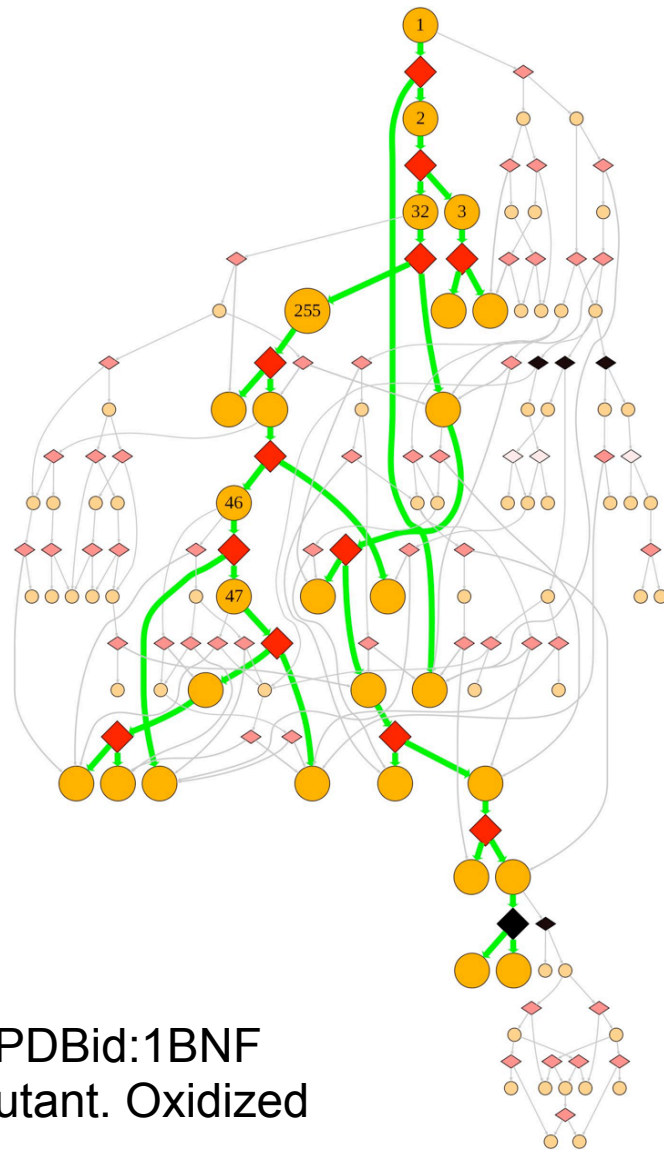
In each of the directed acyclic graphs (DAG) presented here, node 1 is the natively folded state. Circles denote intermediates of unfolding as defined by the GetCuts algorithm. Lines with diamonds are bifurcating directed edges, connected one node to two. Black diamonds are hinges, red diamonds are pivots and white diamonds are breaks, as described in the main paper. The green pathway is the one with the highest traffic in an UnfoldSim simulation. Conditions for the simulation are written on each slide (additional setting can be found in Table 1 of the main paper). Only the edges with at least 10% of the maximum UnfoldSim traffic are plotted.

DAGs can be interpreted in terms of the narrowness of the unfolding pathway. If only the green pathway is present, then GeoFold predicts the folding ensemble to be very tight (and probably more susceptible to mutation). On the other hand, if the DAG contains many pathways, then GeoFold predicts that the pathway is maleable, and probably insensitive to mutation.

Note that some proteins split in the middle at the beginning of unfolding (towards the top of the DAG), while others unfold from the ends, a single linear pathway. Other proteins have several required steps before splitting into multiple pathways -- a bottleneck.

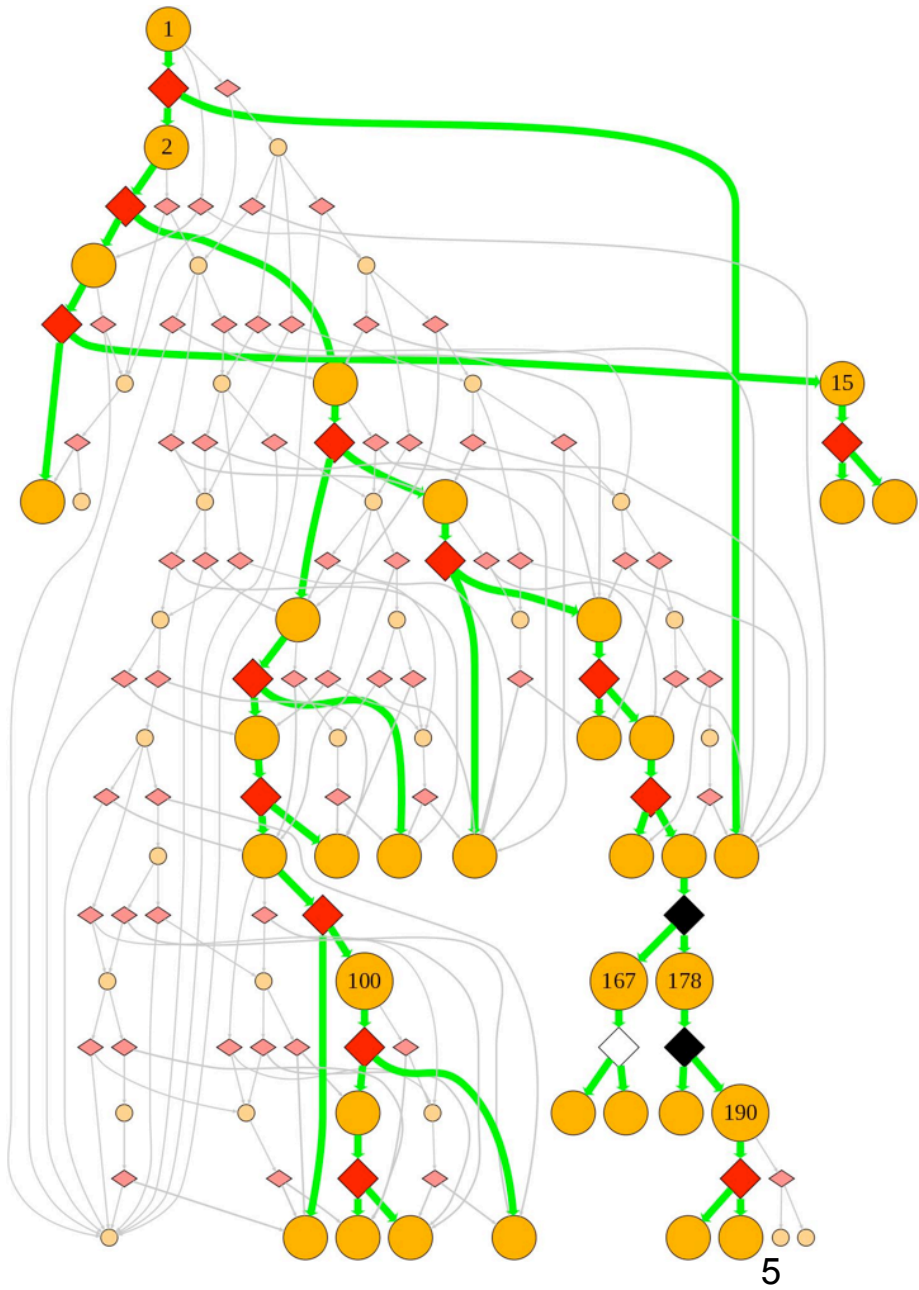


Geofold DAG for PDBid:1BNE
Barnase 43-80 mutant. Oxidized
 $\omega=40$

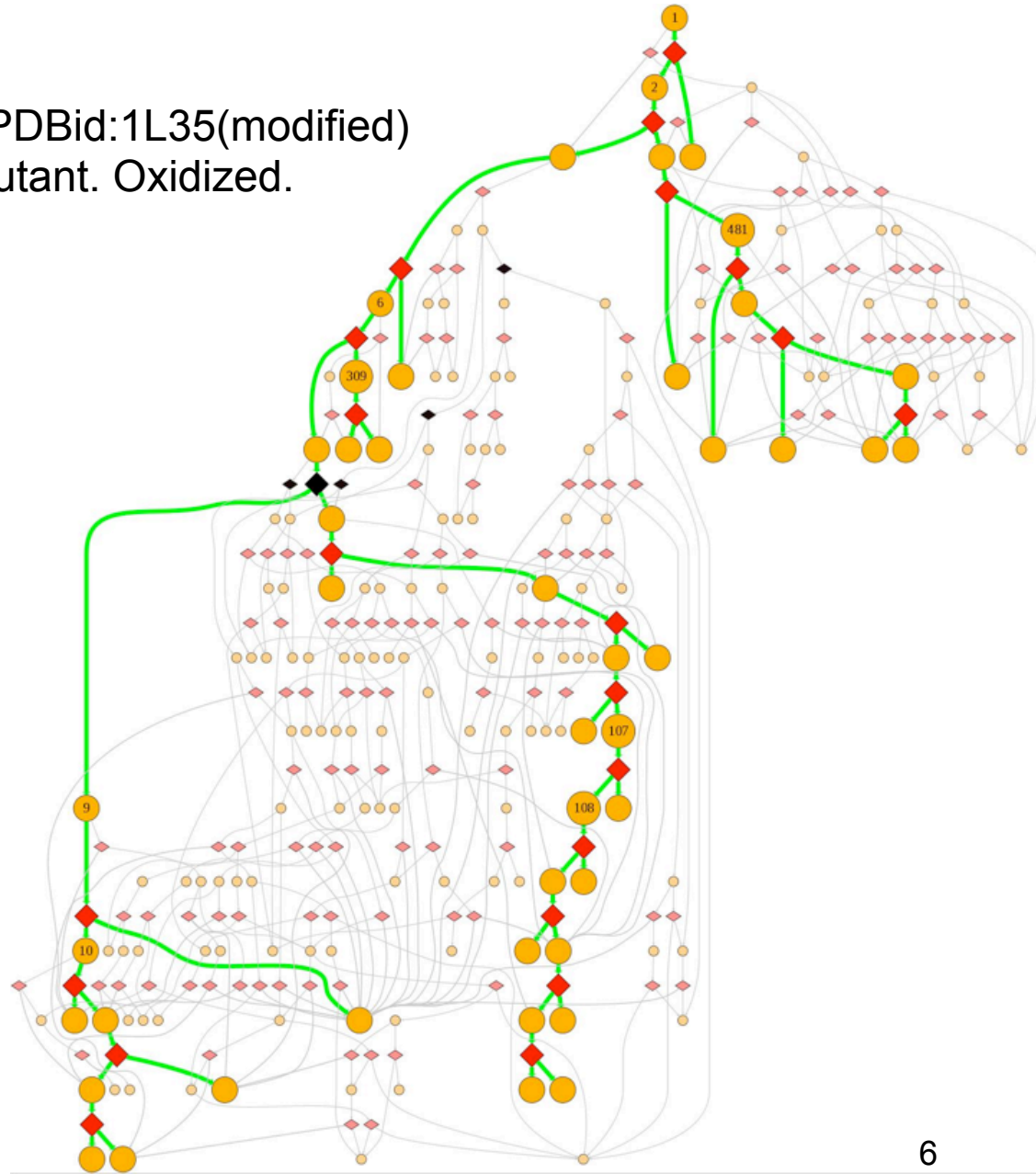


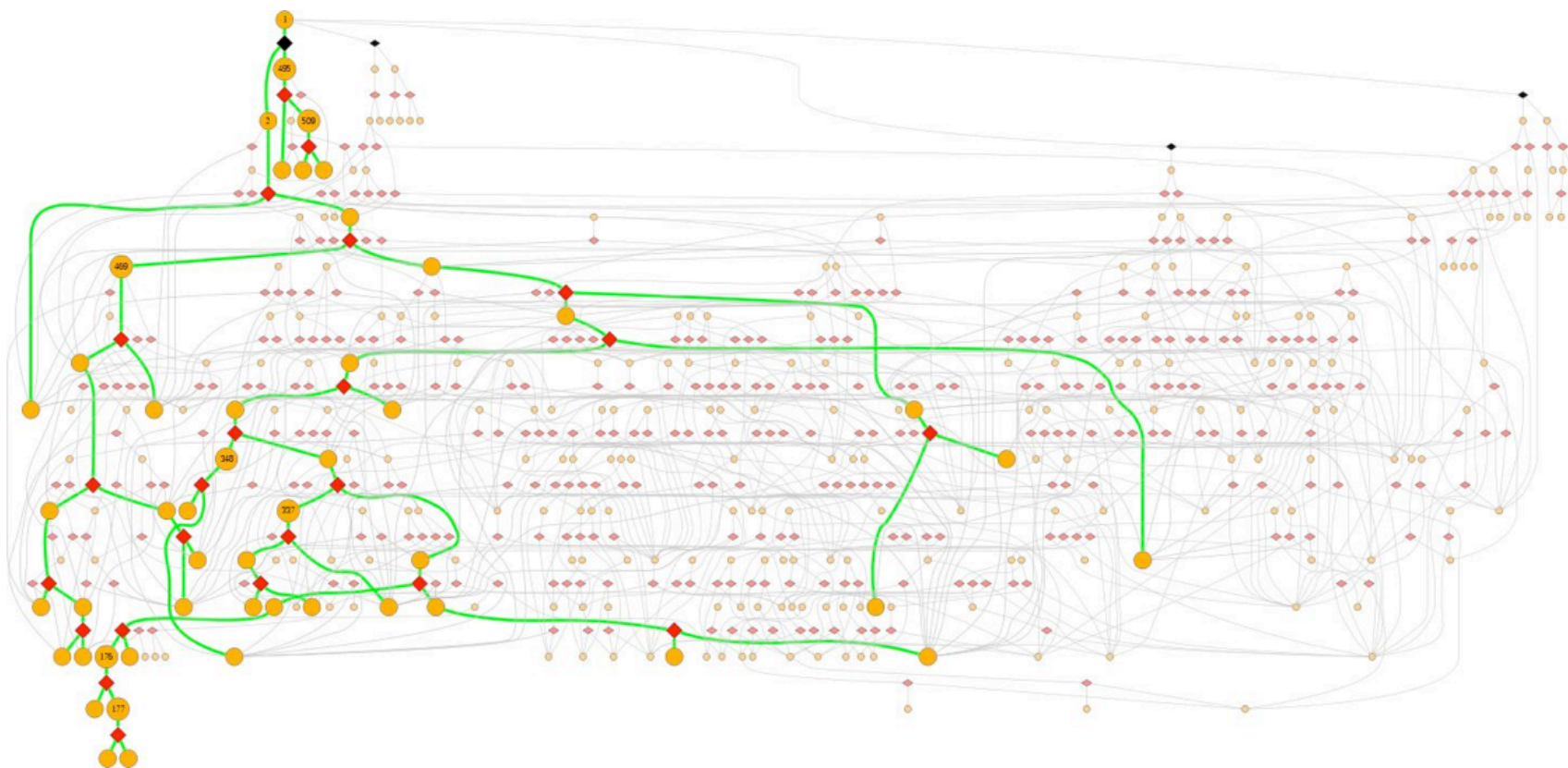
Geofold DAG for PDBid:1BNF
Barnase 70-92 mutant. Oxidized
 $\omega=40$

Geofold DAG for PDBid:1BNG
Barnase 95-102 mutant. Oxidized
 $\omega=40$



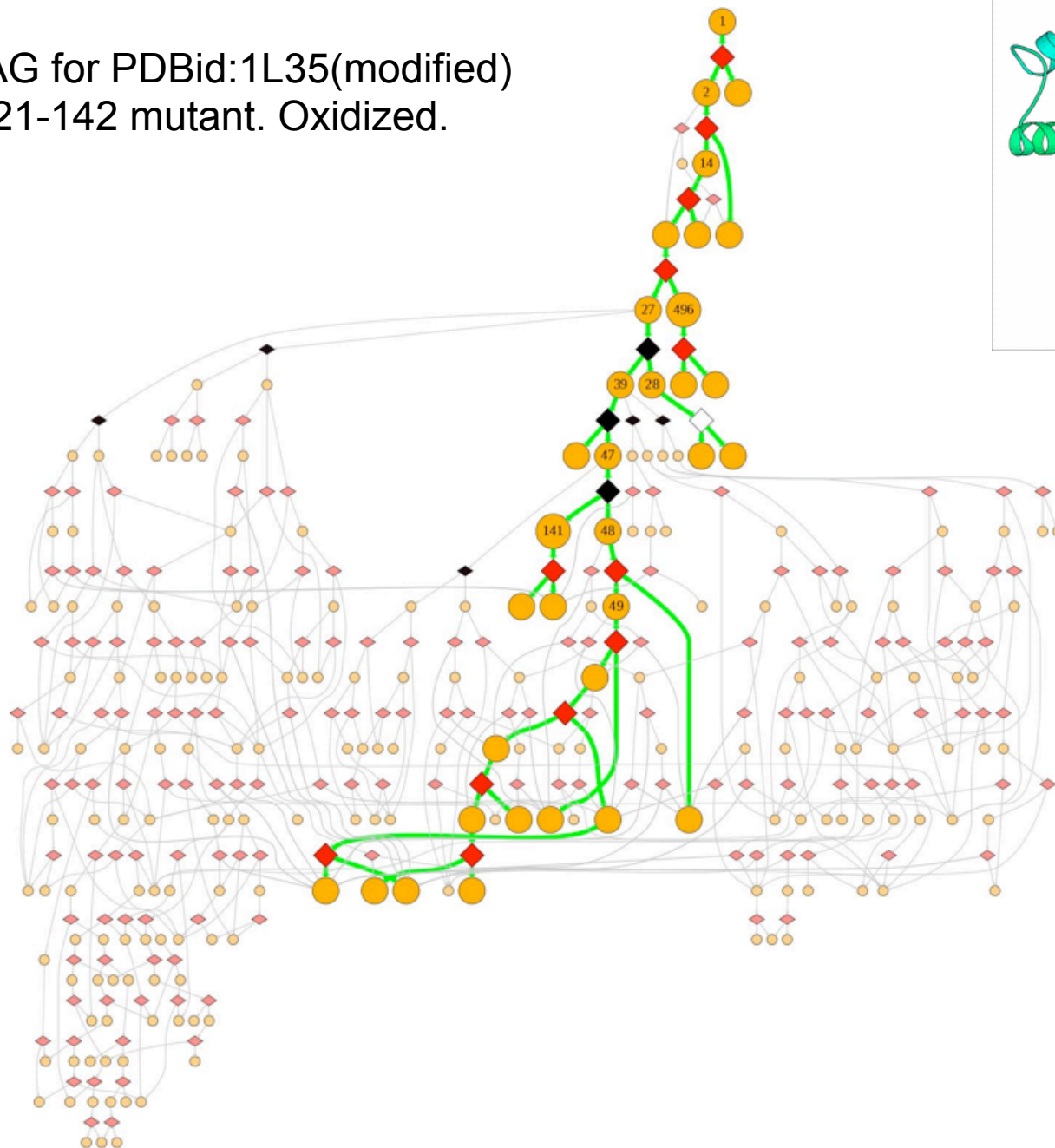
Geofold DAG for PDBid:1L35(modified)
Lysozyme 3-97 mutant. Oxidized.
 $\omega=40$



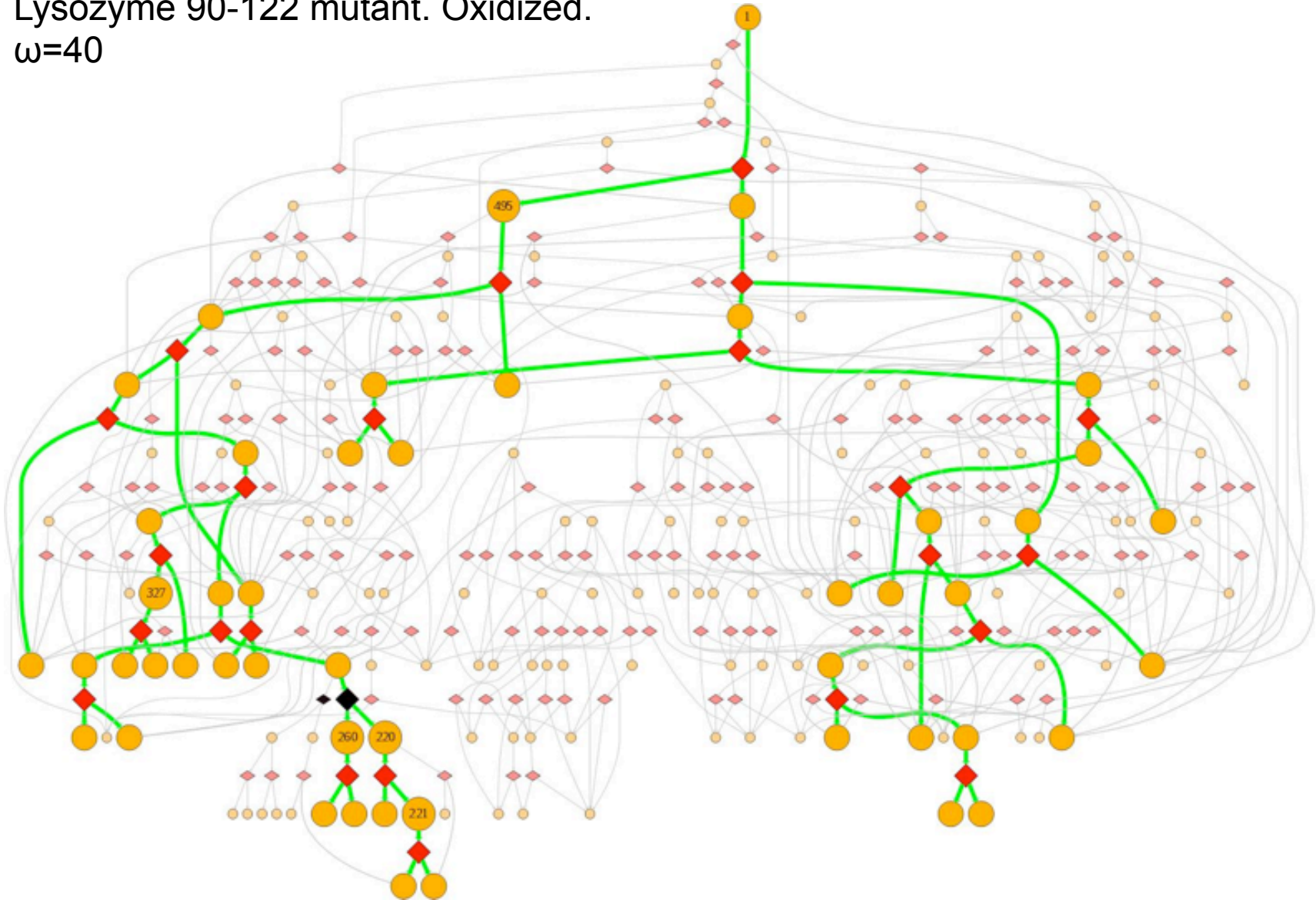


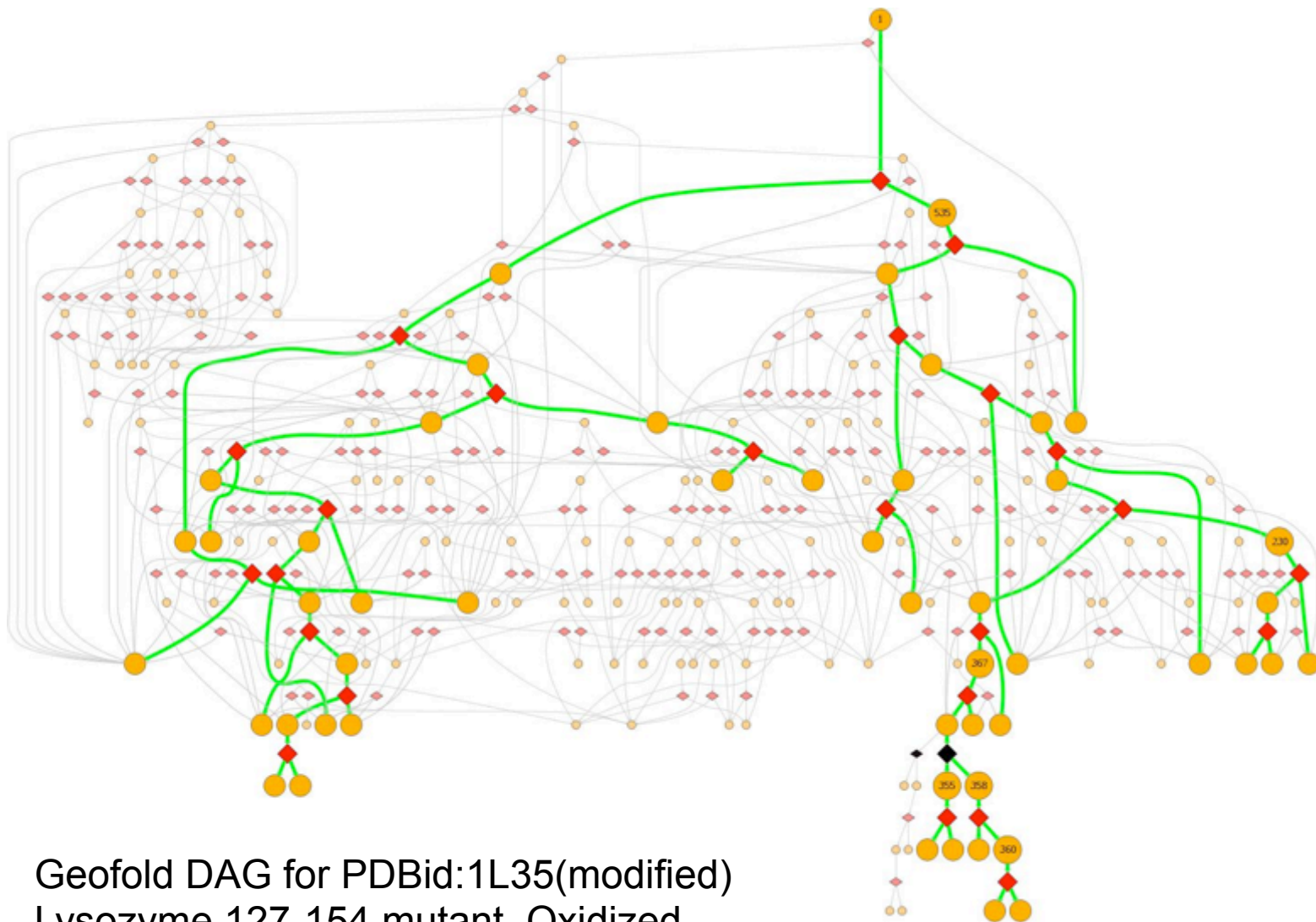
Geofold DAG for PDBid:1L35(modified)
Lysozyme 9-164 mutant. Oxidized.
 $\omega=40$

Geofold DAG for PDBid:1L35(modified)
Lysozyme 21-142 mutant. Oxidized.
 $\omega=40$



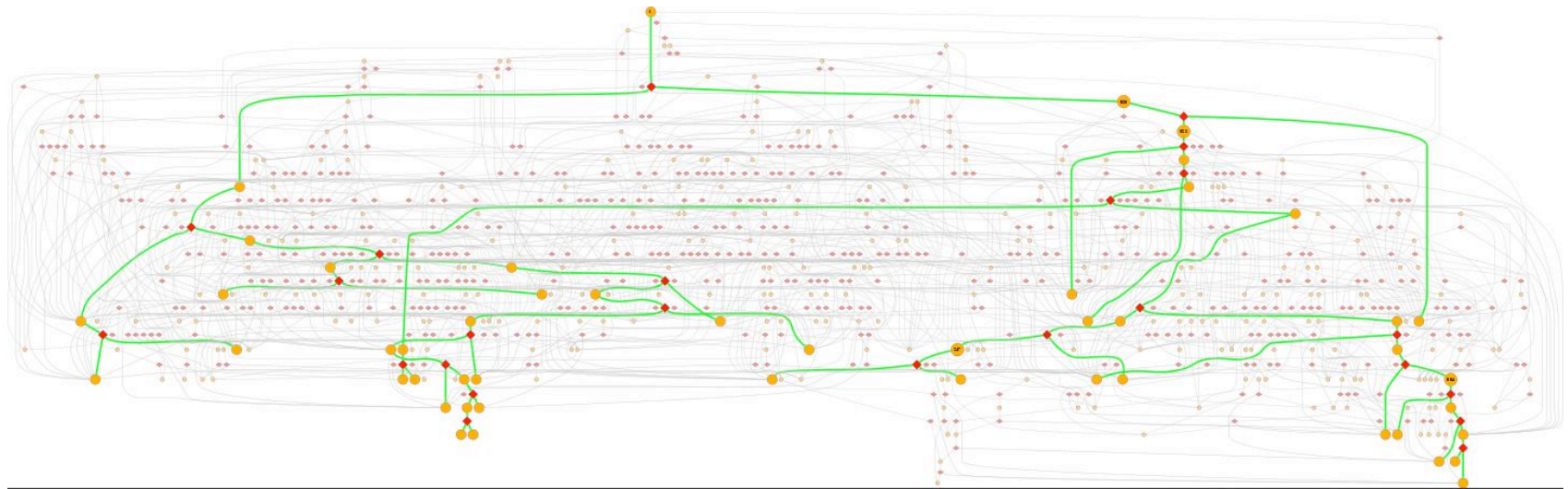
Geofold DAG for PDBid:1L35(modified)
Lysozyme 90-122 mutant. Oxidized.
 $\omega=40$



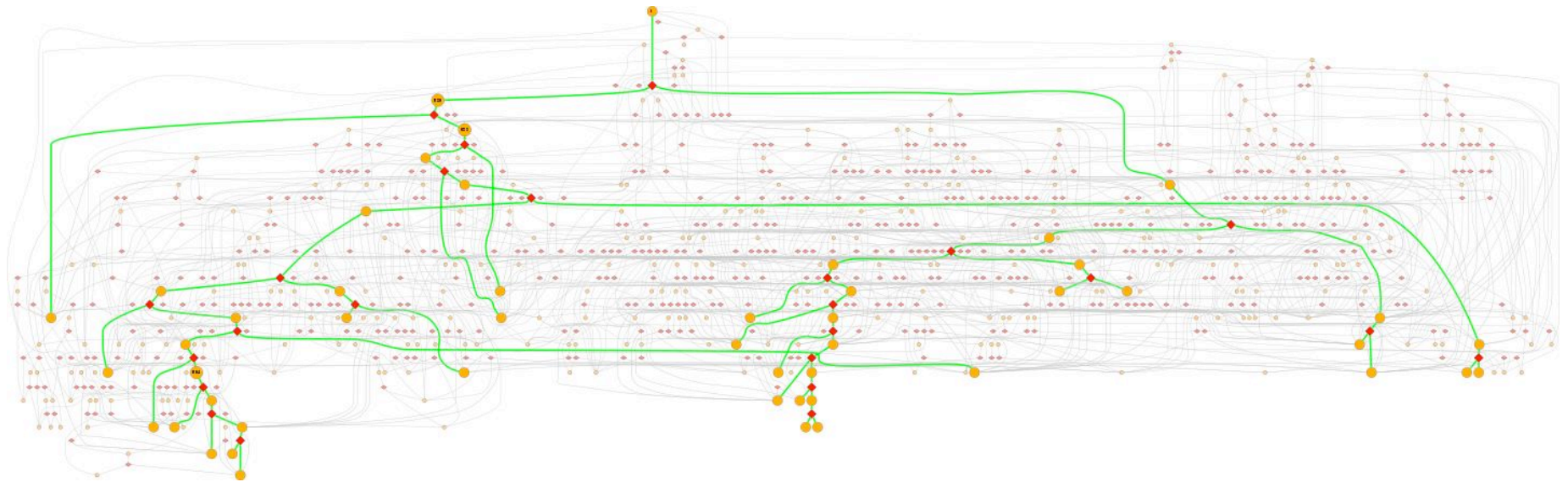


Geofold DAG for PDBid:1L35(modified)
Lysozyme 127-154 mutant. Oxidized.
 $\omega=40$

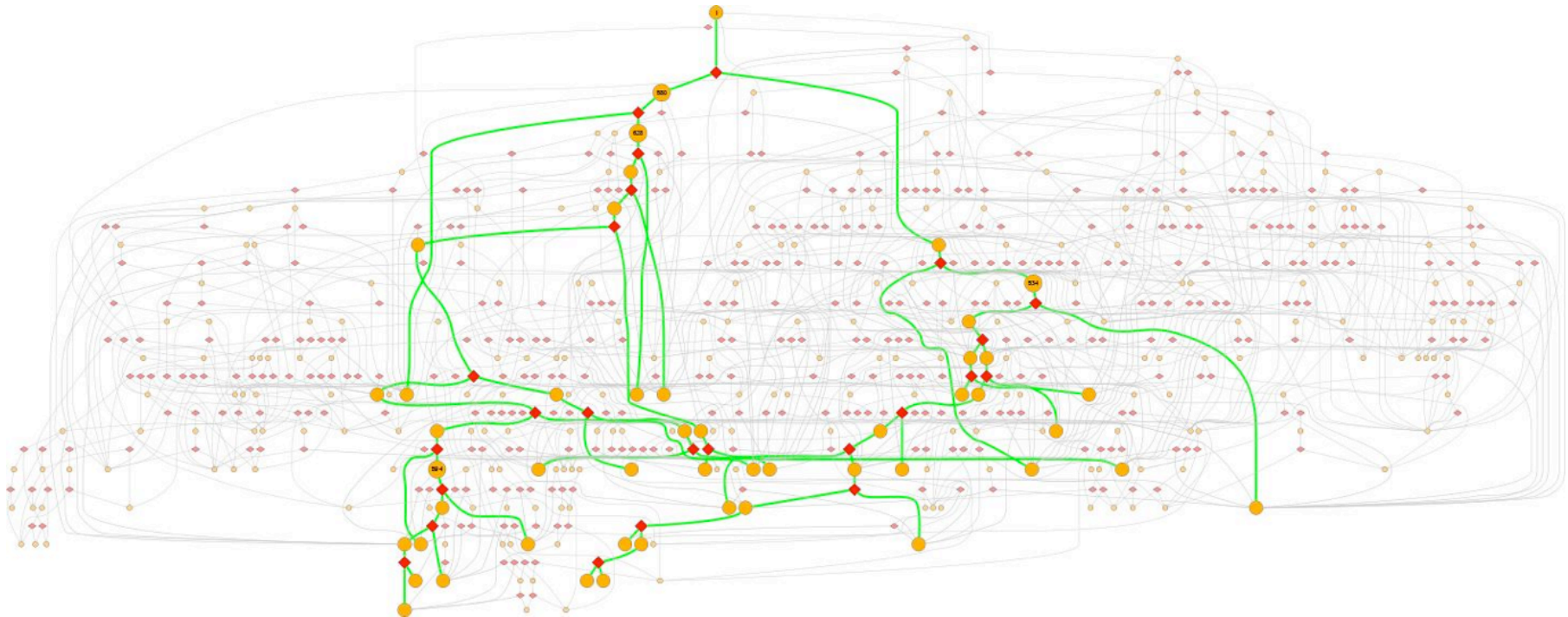
Geofold DAG for PDBid:1LYD
 $\omega=10$



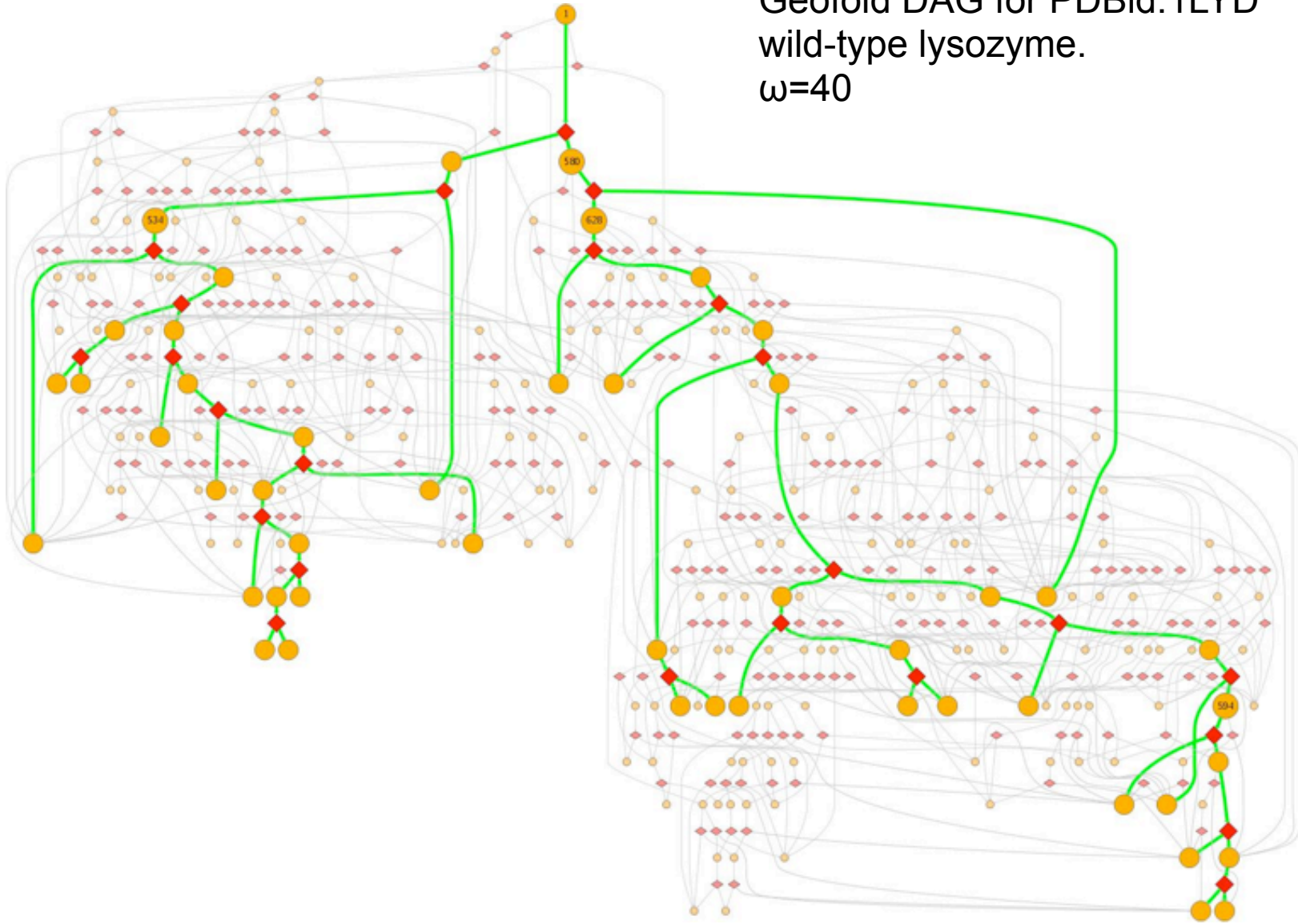
Geofold DAG for PDBid:1LYD
wild-type lysozyme.
 $\omega=20$



Geofold DAG for PDBid:1LYD
wild-type lysozyme.
 $\omega=30$



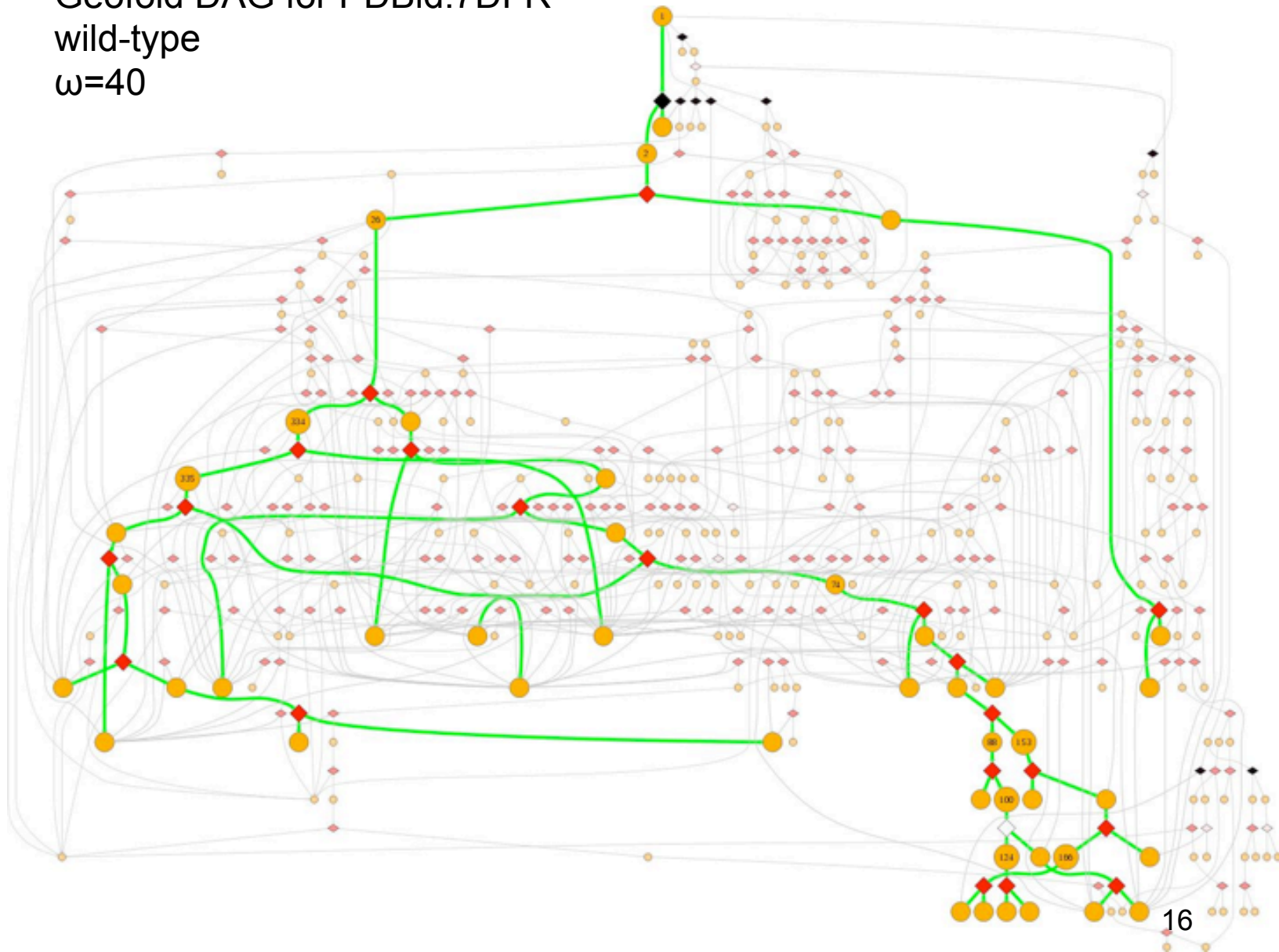
Geofold DAG for PDBid:1LYD
wild-type lysozyme.
 $\omega=40$



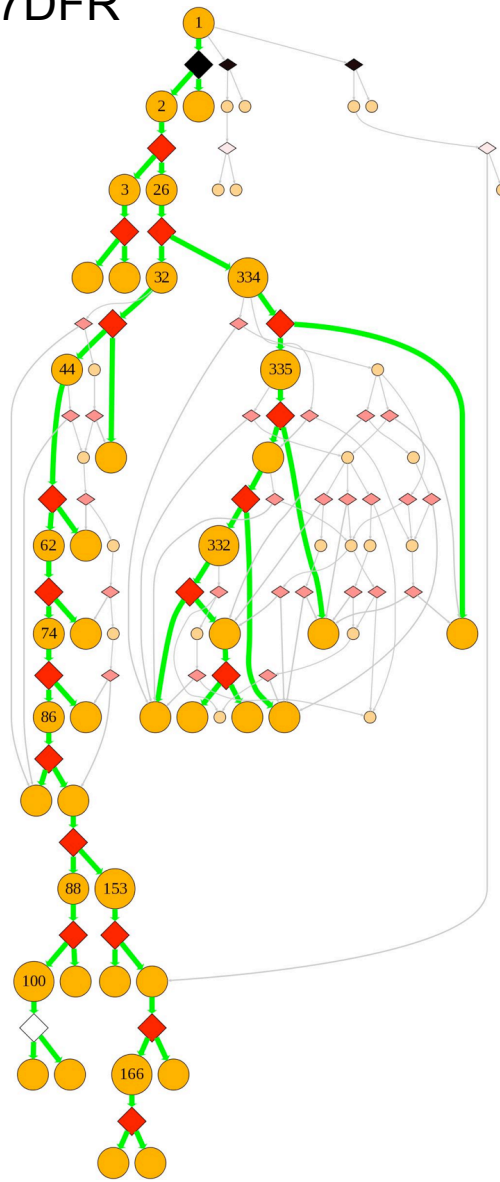
Geofold DAG for PDBid:7DFR
 $\omega=10$



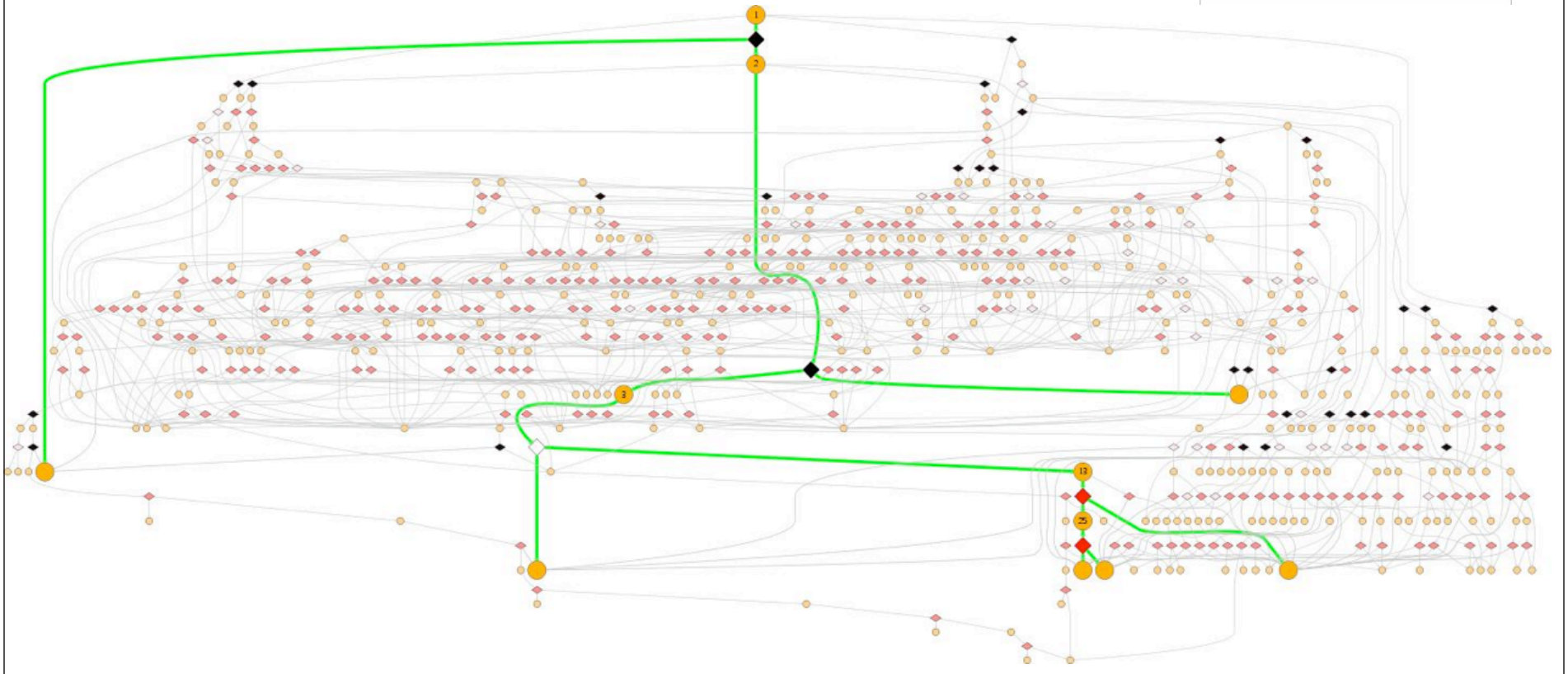
Geofold DAG for PDBid:7DFR
wild-type
 $\omega=40$

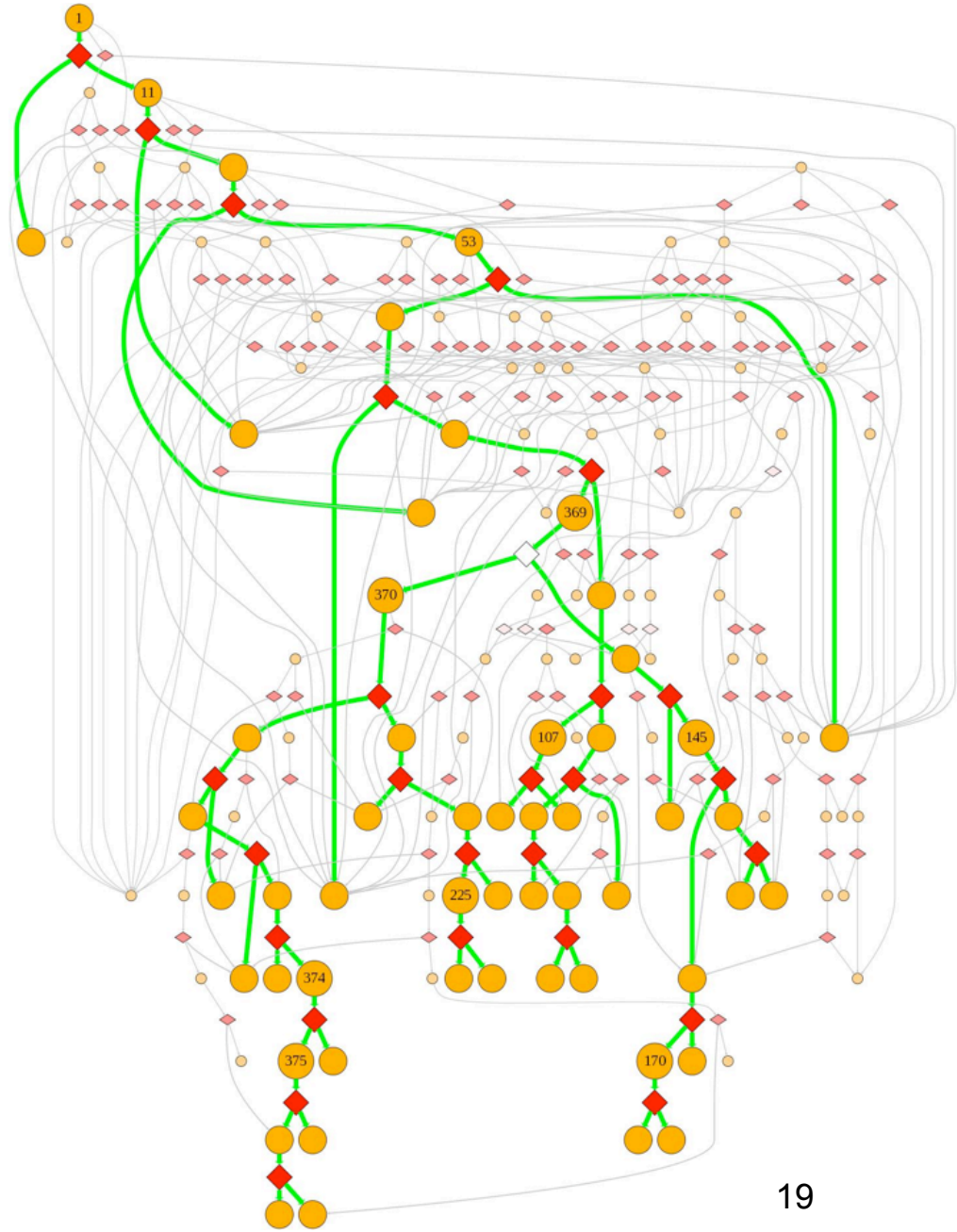
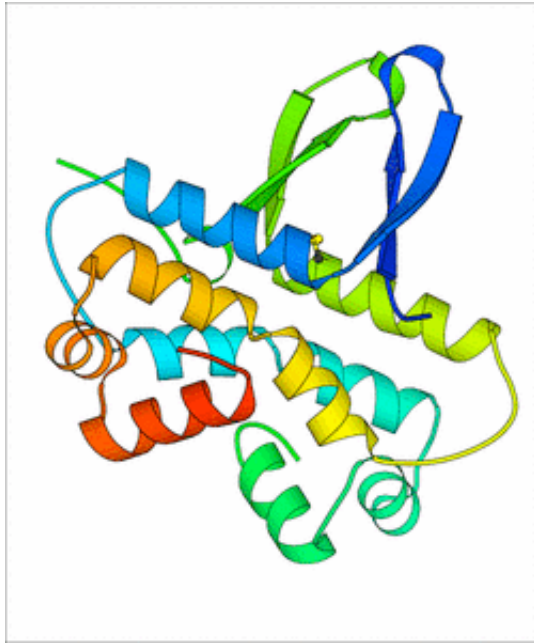


Geofold DAG for PDBid:7DFR
 $\omega=60$



Geofold DAG for PDBid:7DFR(modified)
P39C mutant. $\omega=15$





Geofold DAG for PDBid:3jrh
 wild type FIS
 $\omega=40$

