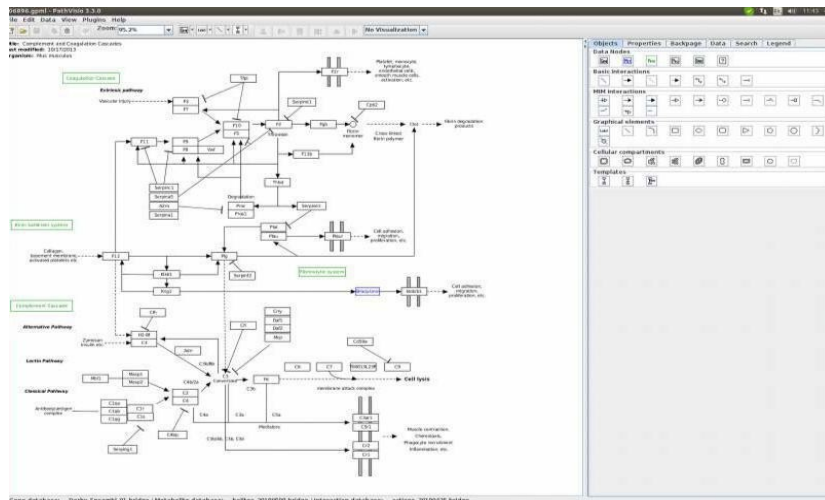


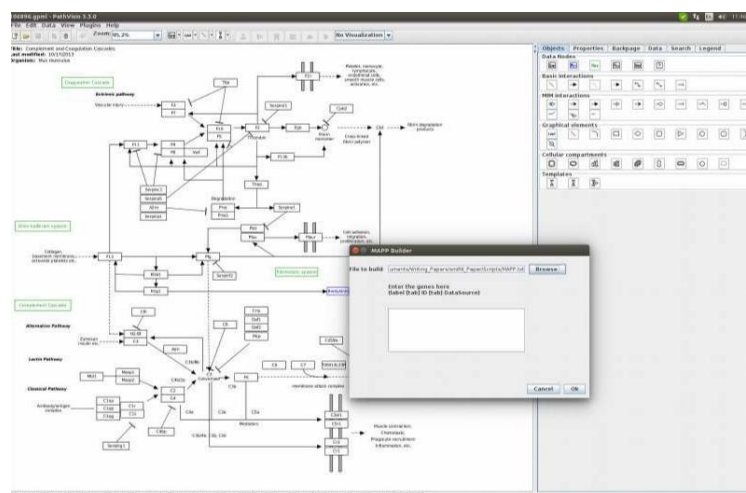
TimiRGeN - Pathvisio GRN creation guide:

1) Open selected pathway in Pathvisio. (<https://pathvisio.github.io/>)
Use the set up instructions found on the pathvisio website. You can download your pathway as a gpml format from wikipathways or use the wikipathways app in pathvisio to import the pathway (1, 2). Can download the wikipathways app here <https://pathvisio.github.io/plugins/wikipathways.html>.

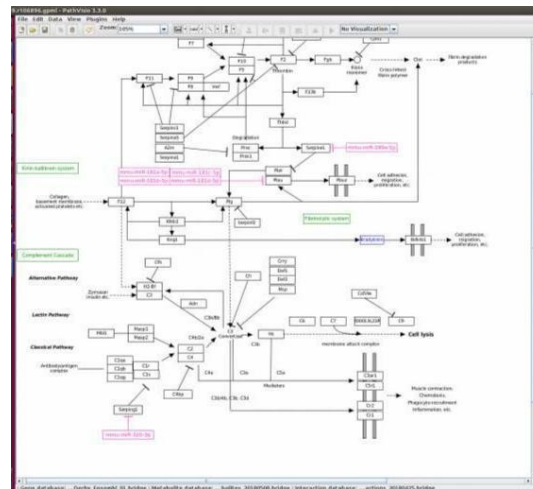


2) If microRNA entrezID/ ensembl ID's are missing, use MGI or ensembl to find these and manually insert them next to correct microRNA. For -5p and -3p clashes, use a .1 or .2 to differentiate.

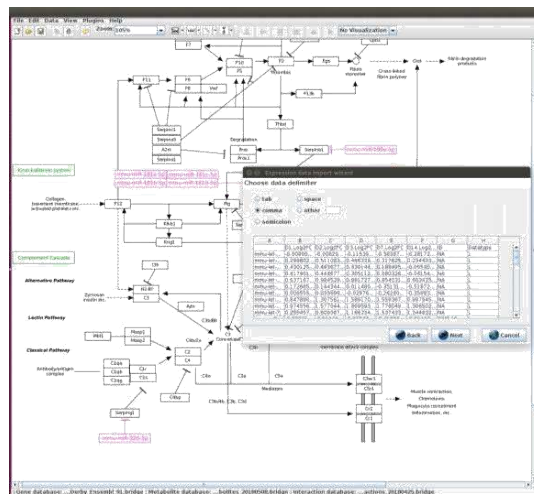
3) Use the MAPP app on Pathvisio to import the MAPP txt file created with TimiRGeN. (<https://github.com/PathVisio/mappbuilder>).



4) Manually place microRNAs where they should be on the wiki pathway..



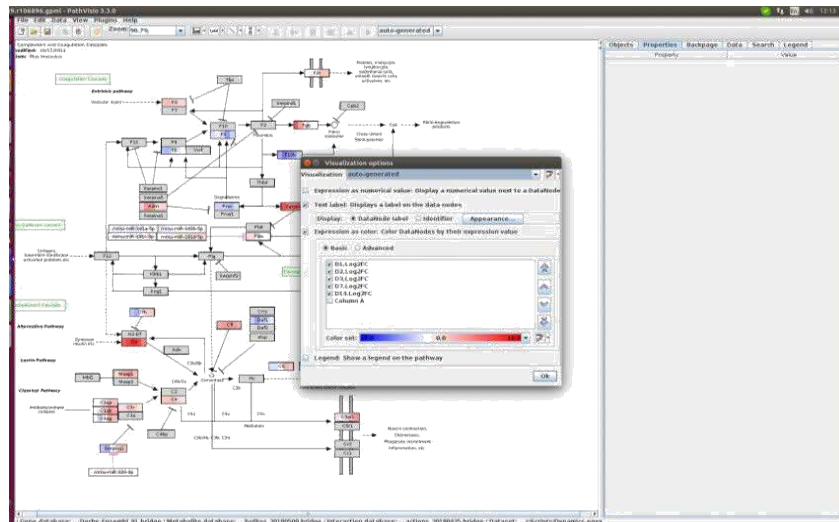
5) Import the dynamics file (Data > Import expression data). Select comma.



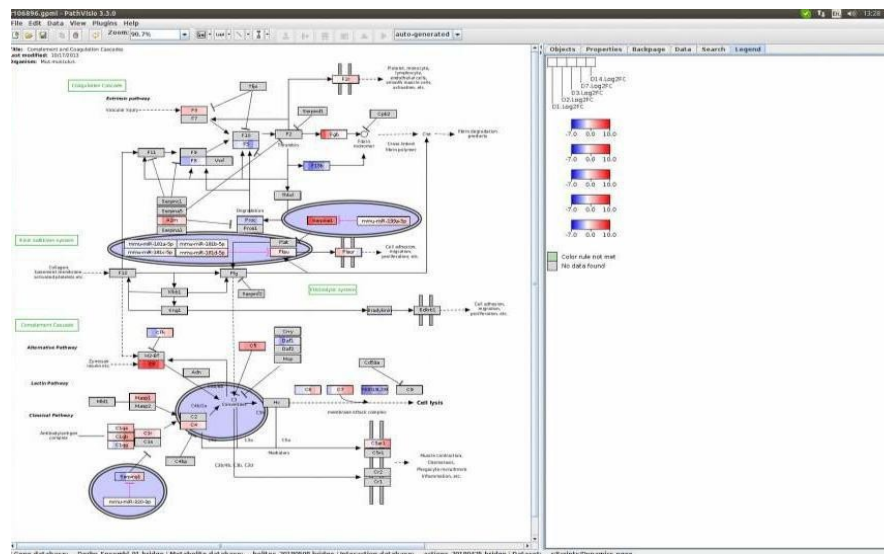
6) Choose Primary identifier column (Green) as ID and column to specify system code as Datatype (red).

ID	Name	System	Datatype
1	1-ADP	1-ADP	1-ADP
2	1-ADP	1-ADP	1-ADP
3	1-ADP	1-ADP	1-ADP
4	1-ADP	1-ADP	1-ADP
5	1-ADP	1-ADP	1-ADP
6	1-ADP	1-ADP	1-ADP
7	1-ADP	1-ADP	1-ADP
8	1-ADP	1-ADP	1-ADP
9	1-ADP	1-ADP	1-ADP
10	1-ADP	1-ADP	1-ADP
11	1-ADP	1-ADP	1-ADP
12	1-ADP	1-ADP	1-ADP
13	1-ADP	1-ADP	1-ADP
14	1-ADP	1-ADP	1-ADP
15	1-ADP	1-ADP	1-ADP
16	1-ADP	1-ADP	1-ADP
17	1-ADP	1-ADP	1-ADP
18	1-ADP	1-ADP	1-ADP
19	1-ADP	1-ADP	1-ADP
20	1-ADP	1-ADP	1-ADP
21	1-ADP	1-ADP	1-ADP
22	1-ADP	1-ADP	1-ADP
23	1-ADP	1-ADP	1-ADP
24	1-ADP	1-ADP	1-ADP
25	1-ADP	1-ADP	1-ADP
26	1-ADP	1-ADP	1-ADP
27	1-ADP	1-ADP	1-ADP
28	1-ADP	1-ADP	1-ADP
29	1-ADP	1-ADP	1-ADP
30	1-ADP	1-ADP	1-ADP
31	1-ADP	1-ADP	1-ADP
32	1-ADP	1-ADP	1-ADP
33	1-ADP	1-ADP	1-ADP
34	1-ADP	1-ADP	1-ADP
35	1-ADP	1-ADP	1-ADP
36	1-ADP	1-ADP	1-ADP
37	1-ADP	1-ADP	1-ADP
38	1-ADP	1-ADP	1-ADP
39	1-ADP	1-ADP	1-ADP
40	1-ADP	1-ADP	1-ADP
41	1-ADP	1-ADP	1-ADP
42	1-ADP	1-ADP	1-ADP
43	1-ADP	1-ADP	1-ADP
44	1-ADP	1-ADP	1-ADP
45	1-ADP	1-ADP	1-ADP
46	1-ADP	1-ADP	1-ADP
47	1-ADP	1-ADP	1-ADP
48	1-ADP	1-ADP	1-ADP
49	1-ADP	1-ADP	1-ADP
50	1-ADP	1-ADP	1-ADP

7) Select a suitable colour palette to represent the time series. The segments will be shown in an order which matches the Dynamic file. (Data > Visualization options)



8) Isolate key parts of the pathway for bottom-up GRN construction. In this example, the interactions of the miR-mRNA target's can be seen to effect the biogenesis of C3 convertase.



References

- 1) Slenter DN, Kutmon M, Hanspers K, et al. WikiPathways: a multifaceted pathway database bridging metabolomics to other omics research. *Nucleic Acids Res.* 2018;46(D1):D661D667. doi:10.1093/nar/gkx1064
- 2) van Iersel MP, Kelder T, Pico AR, et al. Presenting and exploring biological pathways with PathVisio. *BMC Bioinformatics.* 2008;9:399. Published 2008 Sep 25. doi:10.1186/1471-2105-9-399