PhD Diary

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April 5, 2019

Contents

1 Tasks [3/6]

1.1 DONE Create a data set from Christine's images for n-order connections from origin cell

- Moving to longer term goals

1.1.1 TODO Think of exact uses for this first

1.2 TODO Show limits of instability for $\Delta x|y$

- It would be good to show that, for example, greater than 30 minutes and $\Delta x|y$ can be the length of an average cell
- This would mean the network idea could work much faster and better

1.3 DONE Test D_{eff} vector idea

1.3.1 This probably won't work

Because if we make it a matrix, then we make the assumption that all connections to and from a cell are of a similar q, otherwise we aren't recording what's leaving and what's coming in accurately !

Something like this:

```
def diffuse_vectorise(un, g, b, dt, dx2, dy2, a):
    """
    Takes a state, rate of decay, production, delta time, delta space and
    flux of molecule. Uses these data to compute next time state
    """
    return (un[1:-1, 1:-1] + a *
           (((un[2:, 1:-1] - 2 * un[1:-1, 1:-1] + un[:-2, 1:-1]))/dx2 +
            ((un[1:-1, 2:] - 2 * un[1:-1, 1:-1] + un[1:-1, :-2]) / dy2))) *\
        g + b
```

Though, where α should be

$$\alpha = \begin{pmatrix} D_{0,0} & \cdots & D_{0,x} \\ \vdots & & \vdots \\ D_{y,0} & \cdots & D_{y,x} \end{pmatrix} \tag{1}$$

1.4 TODO Look into applying for this course

https://coursesandconferences.wellcomegenomecampus.org/our-events/systems-biology-2019/

1.5 DONE Fill out VPN form and ask Richard to sign off on it

1.6 TODO Come up with questions to ask and answer with proposed models?

1.6.1 QUESTION Is it possible, or is there any use for coming up with probabilistic networks

- These could be inferred from Christine and J's imaging data.

1.6.1.1 Example table

Origin cell connections	avg brightness of 1st neighbours	avg brightness of 2nd neighbours
4	0.5	0.2
2	0.7	0.3
5	0.3	0.1

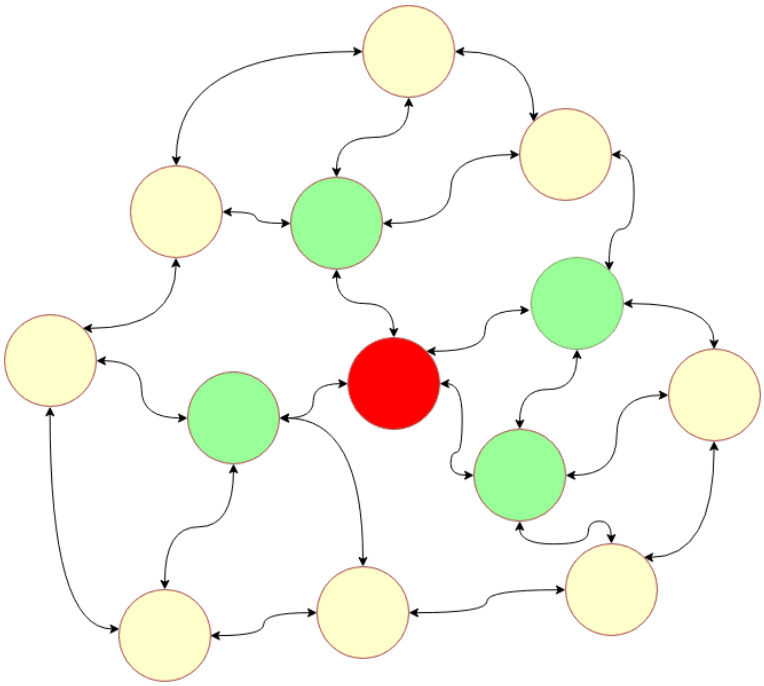

Figure 1: Example of networks, initial cell being red, 1st order green and 2nd order yellow cells

2 Signalling networks course

2.1 Notes

- There are a lot of protein overlaps between pathways (Lu et al. Trends Biochem Sci 2007)
  - Some share core components, some just proteins
- E.g.
  - Input (ligands)
  - Pathway mediators (cross-talk proteins)
  - Output (transcription factors)
- Pathway definitions are not identical
- Curation rules are not uniform
- Cross-talks and overlaps (multi-pathway proteins) cannot be examined (easily)

2.1.1 Types of signalling pathways

- Canonical (e.g. mapk)
- Functional (e.g. inflammation)
- Inferred (e.g. from expression data)
  - Take out what is not expressed and it simplifies everything
- Cellular processes regulating (e.g. autophagy induction)

- Organ-related (e.g. vulva development)
- Disease-related
- Drug-related

Highly overlapping, functionally NOT distinct pathways Comparison or cross-talk analysis between different types of signalling pathways is incorrect

2.1.2 Defining canonical signalling pathways

2.1.2.1 Papers

- 1998 Warkany Lecture: signaling pathways in development (john gerhart)
- The evolution of signalling pathways in animal development

2.2 Case study Korcsmáros et al. [1]

- SignaLink database
  - Korcsmaros et al., Bioifnormatics (2010), PloS ONEe (2011)
- Often interactions are inferred cross species, and report interactions which are never verified
- Key question to ask:
  - Are they physically interacting or are they indirectly interacting

2.3 Lookup

2.3.1 Interactions lookup

- IHOP
- Chilibot
- PSICQUIC interface lookup

2.4 Signal transduction

- Activity flows are directed interactions
- Process descriptions, directed, sequential and mechanistic
- Enzyme substrate interactions - they show directionality

2.4.1 Papers

- Concalves et al 2012 Mol. BioSyst
- Le Novere, Nat Rev Genet 2015

2.5 Software

2.5.1 Reactome

- is for interactions, manually curated and peer-reviewed - FOSS - pathways are hierarchically organised
- Very nice for visualisation

2.5.2 Signor

- Data structure for entities and relationships
- Grabs references for each interaction

2.6 Cytoscape and data analysis for networks

2.6.1 Summary of intro

- Networks are useful
- Transitivity of networks is worth looking into

2.7 Omnipath and Bypath

- https://github.com/deeenes/bioinfo-tools#python-ides

References

[1] Tamás Korcsmáros, Illés J. Farkas, Máté S. Szalay, Petra Rovó, Dávid Fazekas, Zoltán Spiró, Csaba Böde, Katalin Lenti, Tibor Vellai, and Péter Csermely. Uniformly curated signaling pathways reveal tissue-specific cross-talks and support drug target discovery. *Bioinformatics*, 26(16):2042–2050, August 2010. ISSN 1367-4803. doi: 10.1093/bioinformatics/btq310. 00081.