Gerald's Zettelkasten

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Inbox

Information dump while the thoughts are still fresh.

General Overview

Introduction

This is simply an information dump of all the questions and ideas and questions that burn through my mind. A mind-palace if you will, to connect all my ideas into a cohesive-interlinked framework.

Part I

Open Questions

Chapter 1

Bioinformatics

1.1 Metagenomics

1.1.1 Coverage, Depth, Sequencing

Further Investigations

One may create a plot of genome size vs coverage

1.1.2 The deal with spiking

- How much spiking should be done? – most papers only give a ballpark percentage of the community (which I presume requires prior optimization and re-optimization until it becomes the 1% threshold they are after)
- Which is better? To choose spike that can be representative of the sequence? or to choose a spike that is completely unrelated to the environment you are sampling?
- Why does GC skew matter here? What does it really show? Inefficacy of the sequencing platform? – How might we test this?

1.1.3 How much DNA should is representative of a site?

1.1.4 How many reads do we need per site?

Further Investigations

Meta-analysis per journal based on IF perhaps? too subjective?
”Tapering-off” analysis
Power Analysis
Sequence Space Exploration

- Start with alleles of the protein-homologues or SNP sequence space

Chapter 2

Hydrodynamics

2.1 Flow and effluents

Metro Manila

Which effluents flow directly into the Pasig River? Tullahan? Other River systems?
What tributaries specifically though?
What is the flow of these tributaries? Can we simulate them?
Can we have access to the underground sewage system?

Chapter 3

Legal

Chapter 4

Philosophical/Theological

Part II

Notable Information

Chapter 5

Batch effects

5.1 ”Technician Bias”

Part III

Cookbook

Chapter 6

The conundrum of biological sequences

6.1 Entropy-based analysis

The idea here is that biological systems are essentially highly-optimized to maximize entropy in the Universe – it has to if has to retain it's order. Given that part of that increase in entropy, is released from massive amounts of heat generated from the `The Central Dogma of Molecular Biology` itself and its maintenance, information entropy comes into play.

6.2 Evolutionary Tensor Landscape

6.3 Automation for RSS feeds

6.4 Jupyter in Lectures and Workshops

6.5 Amplifying Caffeine

6.5.1 Background: Caffeine and Adenosine

Caffeine is an adenosine receptor antagonist (particularly subtypes A1 and A2). This is competitive binding, meaning both molecules *compete* for a "spot" on the receptor – which is important to note here because **caffeine does not displace adenosine once it's bound**, increasing caffeine intake merely increases the **likelihood of it binding to more receptors vs adenosine** – or in biochemical speak, increases [ES] or the ligand-enzyme complex.
Ultimately this means that when you already have a lot of adenosine bound to its receptor, adding more caffeine won't displace them and will do little to counter the large degree of sleep pressure you experience.
Another consequence of this is as long as caffeine is in your system, once the adenosine either dissociates or is metabolized, caffeine starts binding - and only then, does it prevent adenosine from binding. **In a sense think of it this way, caffeine does not destroy sleep pressure, it slows down it's build-up.**
So I think you already have an idea of what we are cooking today, what if – we get rid of adenosine itself.

6.5.2 Metabolism of Adenosine

The main pathway I am looking at here is the stepwise dephosphorylation of ATP $\rightarrow$ ADP $\rightarrow$ AMP $\rightarrow$ Adenosine – which is necessary for many metabolic processes most often as part of a coupled reaction. **The cooking part is** to leverage `Le Chatelier's Principle` i.e. drain ATP which either

- Reverses the reaction
- Depletes the production of Adenosine via this pathway

For example, one may donate blood before drinking caffeine. Donating blood was used as an example as it is considered safe (relatively, depending on how healthy you are of course) – but draining blood in the body leads to erythropoiesis, leucopoiesis,, cytokine signaling, platelet activation and tissue repair (for the needle wound) – all requiring large amounts of ATP. While RBCs may not contain nuclei, their precursors do and what do nuclei have? A LOT of DNA, and DNA replication is a massive ATP sink.

Disclaimer please don't donate blood then start deadline lifting, you'll faint from hypotension lmao.
Other ways to drain ATP indirectly

1. Ion transport pumps that convert ATP free energy into electrochemical gradients
    - Na/K ATPase pumps
    - SERCA Ca^{2+}
2. Uncoupling proteins (UCPs) in the mitochondria – think brown fat ([TBA])
3.

But there are also two other ways via elimination of Adenosine itself

- **Adenosine deamination**
  Adenosine → Inosine → Hypoxanthine → Xanthine → Uric Acid
- **Adenosine Phosphorylation** (back to AMP)

Now the problem with using the first one is that high-levels of uric acid can lead to kidney stones and gout (need to check the literature on the direction of causality on this one [TBA]).
Another obvious side-effect is that for some individuals, it might exacerbate restlessness, anxiety, and/or insomnia. **But speaking of increasing insomnia**, `Russian sleep experiment creepypasta` anyone? Increased metabolic stress may also play a significant role – especially for something like (glycolysis inhibition like shunting everything into PPP).
And as with all drugs, the body will likely overcompensate (if a drug or cocktail is created), that would lead to dependence – this is not your normal caffeine crash since the body might respond by increasing the adenosine receptors at a higher rate (need to research destroying vs inhibition on enzyme overproduction [TBA]).
Moderate AMPK activation

6.5.3 Theoretical use case

Places wherein you would need emergency wakefulness such as space travel or military operations.

If you were to use the AMPK activation pathway, this could lead to weight loss (which may be unwanted and uncontrolled) – due to your body in heightened catabolic state.

6.5.4 Further Questions

How does it differ from injecting people with adrenaline?
How would affect drunk drivers? Will the increased alertness be enough to mitigate the effects of alcohol?

Chapter 7

Data visualizations

7.1 The Hive visualization

7.2 Raw reads Manhattan

Sites vs E-value (because it’s more dependent on reference database than P-values)

Chapter 8

A Zettelkasten for scripts

Just pull, the strings themselves, are a pipeline.