Computational Methods in Metagenomics and Microbiome Research

0368-3116-01

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School of Computer Science
Semester B, 2019
Let me know who you are ....

1. Name
2. Degree (undergraduate, MSc)
3. Background (CS/Biology)
4. Registered / not registered
5. Why are you here? Have you ever heard about the microbiome? Metagenomics?
6. Place your bet:
   What is the total number of bacteria in/on the human body?

Welch et al., 2017
Who am I?

- Faculty at Computer Science & Medicine, TAU
- Until 2018: Faculty at Genome Sciences & CS, UW
- Training: CS; Physics; Hi-tech; Computational/mathematical Biology; Complexity
- Interests: Metagenomics; Human Microbiome; Complex networks; Computational systems biology

http://www.borensteinlab.com/
The Seminar’s ‘Mission Statement’

Seminar on computational methods in metagenomics and microbiome research

**Domain Knowledge**
Learn key algorithms/methods developed for processing and analyzing metagenomic data and for accurately mapping the composition of the human microbiome and its role in human health.

**Science Communication**
Practice and master the art of scientific presentation, including slide preparation, presentation skills, talk delivery, and scientific discussion.
Outline

About the Seminar

Tips for Giving a Good Talk

A Very Brief Background about Microbes, Microbiomes, and Metagenomics

Q&A
Outline

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Q&A
Seminar Format

- **Student presentations!!**
  - 1-2 students per paper
    * (when 2 students present the same paper, both should understand everything and the presentation should be split evenly and logically)
  - Talk: Hebrew or English
  - Slides: English
  - Paper selection: “First come first served”, or “Random Rank Preference Selection”
- **Feedback**
- **Discussion**
In Your Presentation:

 Emphasize the main task the paper aims to address

 Cover the required comp/bio background
   Don’t lose your audience

 Focus more on methods than on results
   You will sometimes need to dig deep for the methods (methods sections, supplementary materials, previous papers)
   Don’t leave ‘black-boxes’
   The paper may contain more than you can cover; choose what to include (and what to drop) wisely

 In the end, summarize
   Main results, importance, weaknesses, future work

 Add something original
   Thoughts, ideas, concerns
Feedback and Discussion

- Feedback about presentation:
  - Everyone (we are all expert listeners)
  - Likes and dislikes
  - What was clear, what wasn’t
  - Be genuine but kind and constructive

- Discussion about the paper
  - Speaker should prepare 2 or 3 discussion points
  - Aim to discuss what’s NOT in the paper (hidden rationales, future directions, applications, concerns, …)
Class Structure

- When presenting one paper per class:
  - 1:10 Start talk
  - 2:00-2:10 Break
  - 2:30 End talk
  - 2:30-3:00 Feedback/Discussion

- When presenting two papers per class:
  - 1:10 Start talk 1
  - 1:50 End talk 1
  - 1:50-2:00 Feedback/Discussion
  - 2:00-2:10 Break
  - 2:10 Start talk 2
  - 2:50 End talk 2
  - 2:50-3:00 Feedback/Discussion
קביעת הציון הסופי

- הבנת החומר: 40%
- הצגת החומר: 40%
- השתתפות פעילה בסמינר: 20%
- בונוס מקורי: עד 10%
- בונוס משכימי קום: עד 5%
- חירגה המח紊: עד 10%

Kick off חובת נוכחות בסמינר
Website

- [http://borensteinlab.com/courses/TAU_CS_3116_B_19/](http://borensteinlab.com/courses/TAU_CS_3116_B_19/)

- Print your slides before class

- Send me your slides after class
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Giving a Good Talk

- Partly innate but largely an acquired skill
  - Practice makes perfect
- Part science, but also part art
  - Lots of resources, rules, dos and don’ts, best practice guidelines
  - … but, every rule has exceptions
  - If it works, it works

Identity 2.0 Keynote

https://www.youtube.com/watch?v=RrpajcAgR1E
Presentation – General Tips

- **Be clear!!!!**
  - If your audience comes out of the talk with a feeling that you are really smart but they didn’t really get what you talked about, you failed in your mission!

- **Grab your audience’s attention (and don’t lose it)**

- **Structure your talk**
  - Have a clear beginning, middle, and end
  - Section your talk and highlight transitions (verbally and via slides)
  - Use a ‘home slide’

- **Provide intuition, examples, clear definitions**

- **Use mostly slides, and the board sparingly**

- **Make contingencies in case you’re out of time**
The 3 Rules of a Good Presentation

- Rehearse your talk!
- Rehearse your talk!
- Rehearse your talk (and time it)!

A few other rules/suggestions:
- Record yourself and listen
- Present to friends and family
- Know your next slide (even if you use ‘presenter mode’)
- Write down some of the your script
- But don’t over rehearse
Slide Design: Dos and Don’ts 1

- Use the slide’s real-estate wisely
- Avoid clutter (and be generous with white space)
- If you are not going to take the time to explain it, don’t include it
  - (e.g., image panels, labels, equations)
- Avoid text-heavy slides (like this one)
- Try to include a simple image on every slide
- Use available space but avoid narrow margins (like this one).
Slide Design: Dos and Don’ts 2

- Be (very) mindful about fonts
  - Prefer easy to read fonts
  - Size!!!

- Be (even more) mindful about colors
  - Think about visibility, contrast
  - Remember the color-blinds

- Be mindful about animation
  - Too much (or too animated) can be distracting
  - But often animation is a powerful tool
  - Build your slide progressively (example: plots)

- Be consistent in titles, visuals, colors, etc.

- Don’t be sloppy
Presentation – Resources

- Philip E Bourne’s “Ten Simple Rules for Making Good Oral Presentations” (paper)
  https://journals.plos.org/ploscompbiol/article?id=10.1371/journal.pcbi.0030077

- Susan McConnell’s “Designing effective scientific presentations” (video)
  https://www.youtube.com/watch?v=Hp7Id3Yb9XQ

- Uri Alon’s “How To Give a Good Talk” (paper)
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Why microbes?
Most abundant organisms on earth

- 1 gram of soil: $10^{10}$-$10^{11}$ microbes
- 1 nonillion microbes in the oceans
  
  \[ 1\ \text{nonillion} = 1000000000000000000000000000000 \] 
  
  \[ (= 240\ \text{billion}) \]

Most diverse organisms on earth

- Soil (1g): 6,000-50,000 species
- In total: $10^8$-$10^9$ species (and maybe $10^{12}$)
Microbial communities
Microbes live in the darndest places
The Human Microbiome: Our inner ecosystem
1. Supporting interdisciplinary research to answer fundamental questions about microbiomes in diverse ecosystems.

2. Developing platform technologies that will generate insights and help share knowledge of microbiomes in diverse ecosystems and enhance access to microbiome data.

3. Expanding the microbiome workforce through citizen science and educational opportunities.

New Public and Private Investments in Microbiome Research
Antony van Leeuwenhoek (1632–1723)

Big fleas have little fleas,  
Upon their backs to bite ’em,  
And little fleas have lesser fleas,  
and so, ad infinitum.  

Jonathan Swift
“Though my teeth are kept usually very clean, yet when I view them in a magnifying glass, I find growing between them a little white matter, as thick as wetted flour: in this substance though I could not perceive any motion, I judged there might probably be living creatures.

I therefore took some of this matter and surprize perceived that the aforesaid matter contained very many small living animals, which moved themselves very strangely ...
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I therefore took some of this flour ... and then to my great surprize perceived that the aforesaid matter contained very many small living animals, which moved themselves very strangely ... 

The number of these animals in the scurf of a man's teeth are so many, that I believe they exceed the number of men in a kingdom. ...”
We are mostly microbes!

~90% of the cells in our body are non-human
A typical hand surface harbors >150 species

- Hand washing affects composition (but not diversity)
- Women have significantly higher diversity than men
- Your left hand shares only ~17% of its species with your right hand
- Your hand shares only ~13% of its species with the hand of the person next to you
A Microbiome Fingerprint

Fierer et al., PNAS, 2010

- Indiv. #1 - keyboard key
- Indiv. #1 - fingertip
- Indiv. #2 - keyboard key
- Indiv. #2 - fingertip
- Indiv. #3 - keyboard key
- Indiv. #3 - fingertip
The Skin Microbiome

Hi-Resolution Skin Microbiome Survey

Bacterial data (16s)

Shannon diversity maps

Amina Bouslimani et al. PNAS 2015
The Human Gut Microbiome

- Hundreds of species!
- 100 trillion microbes! (weighing ~3-4lb)
- 150x more genes (~3,300,000)
- Commensal
  - Harvests energy from diet
  - Reduces exposure to toxins
  - Primes the immune system
  - Resists pathogens
The Human Microbiome 2018

We are mostly microbes

Complex and diverse

Highly variable

Crucial processes
B. cellulosilyticus
4 Bacteroides
B. caccae
C. aerofaciens
C. scindens
R. torques
autofluorescence
Microbiome Variation Over Time

Jeremy E. Koenig, 2010
Ottman et al., 2012
David et al., 2014
Microbiome Variation Across Hosts

American Gut Project
Metagenome-wide association studies

Taxonomic profiling

Functional profiling

Controls
Cases

Taxonomic shift

Functional shift

Metagenome-wide association studies
Metagenome-wide association studies

Type 2 diabetes

- Food intake ↓
- Blood glucose ↓

- Metformin

- Intestimabacter spp. ↓
- E. coli ↑

Colorectal cancer

- Red meat ↑
- Vegetables, fibre, fruits ↓

Bacteria that are associated with colorectal cancer
- Fusobacterium spp.
- Parvimonas spp.

Cystic fibrosis

Butyrate catabolism

Hoffman et al., 2014, Manor et al., 2016
Association with disease

- Obesity
- T2 Diabetes
- Hay fever
- Arthritis
- Autism
- Asthma
- colorectal cancer
- Metabolic disorder
- Rheumatoid arthritis
- Alzheimer's disease
- Liver cirrhosis
- Crohn's disease
- Chronic fatigue syn’
- Multiple sclerosis
- Cardiovascular diseases
- Ulcerative colitis
- Diarrhea
- Depression
- Anxiety
- Gastric ulcers
- Malnutrition
- Cystic fibrosis
- Celiac disease
Cause or Effect

- Obesity

Ley et al., PNAS, 2005

Turnbaugh et al., 2009

Ridaura et al. Science, 2013
Next Class:

From Significance to (Computational) Challenges
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