COGS 1: Spring 2019

Section **C**, Week 4

Professor Boyle	*mboyle@ucsd.edu*	Friday, 2-4 pm	CSB 130
Lauren	*lcurley@ucsd.edu*	Tuesday, 10-11 am	CSB 225
Lexi D.	*adalenco@ucsd.edu*	Tuesday, 12:30-1:45 pm	Sun God Lounge
Elena	*edreisba@ucsd.edu*	Thursday, 1-2 pm	CSB 114
Adrian	*ajm033@ucsd.edu*	Wednesday, 5-6 pm	CSB 114
Audrey	*aberardi@ucsd.edu*	Tuesday, 4-5 pm	CSB 114
Devansh	*d4agarwa@ucsd.edu*	Monday, 4-5 pm	CSB 114
Lori	*rol044@ucsd.edu*	Monday, 10-11 am	CSB 114
Lexi F.	*adfrankl@ucsd.edu*	Thursday, 4-5 pm	CSB 114

Important Information

- **Midterm 1**
  - Format: Multiple choice + short answer
  - Midterm 1 is on Tuesday April 30th (Week 5)
    - Review session during lecture on Thursday
      - Bring your questions!

- **Extra Credit**
  - EC quizzes are based on assigned readings
    - Taken on TritonEd
    - Next week's EC quiz is the DAY AFTER your midterm!

**How Babies Think*
*(*EC Prereading quiz: opens on TritonEd Wednesday, May 1 @ 4pm – Tuesday, May 2 @ 10am.*

Last Week's Topics

- Lecture 5 | Dr. Mukamel: Brain Cell Diversity and Epigenetics
- Lecture 6 | Dr. Rangel: Neuronal Regeneration

Lecture 5 | Review Questions (1 of 5)

Vote!!

1. How do cell types within the CNS differ?
2. What is epigenetics?
    a. How do cells become distinct despite having the same genome?
    b. What are histones?
3. What are the basic levels of organization in the genome?
4. How is epigenetics analogous with grammatical punctuation? What is DNA methylation? What is its function?

Lecture 5 | Review Questions (2 of 5)

Vote!!

5. How can methylation affect phenotype?

6. Do epigenetics change over time? Or are they permanent? Why?

7. What is shotgun sequencing?

8. How do the levels of CG and non-CG methylation change throughout a human's life and in different cell types?

9. How do epigenetics play into the debate of nature vs. nurture?

10. What are the similarities and differences between neural networks and gene networks?

Lecture 6 | Review Questions (3 of 5)

Vote!!

11. Is the number of neurons in our brain constant over lifetime?
    a. What is an estimate of the number of neurons in adult brain?
    b. What events can cause a change in the number of neurons?
12. What are the two main neurogenic regions in human brain?
13. What are the stages of new neuron development?
    c. What happens at each stage?
14. How can we quantify neuron proliferation and survival? (doublecortin and BrdU)

Lecture 6 | Review Questions (4 of 5)

Vote!!

15. What are some factors that can affect the proliferation/survival rate of neurons?

    a. Does increased in neuron proliferation also mean increased in neuron survival?

16. What are the major functions of the hippocampus and dentate gyrus ?

17. What is a hypothesized function of adult-born cells in the hippocampus?

    b. How do the experiments described in lecture support this hypothesis?

Reading | Review Questions (5 of 5)

Vote!!

18. What are some negative effects of genetic mutations?
19. What does the field of epigenetics concentrate on?
20. How did experimenters make the parent mice afraid of certain smells? What effects does this have on the parent mice and their offspring?
21. What can be said about famine and disease?
22. Give examples of epigenetic changes and how they affect risk of disease (e.g. during the famine).

Lecture 5

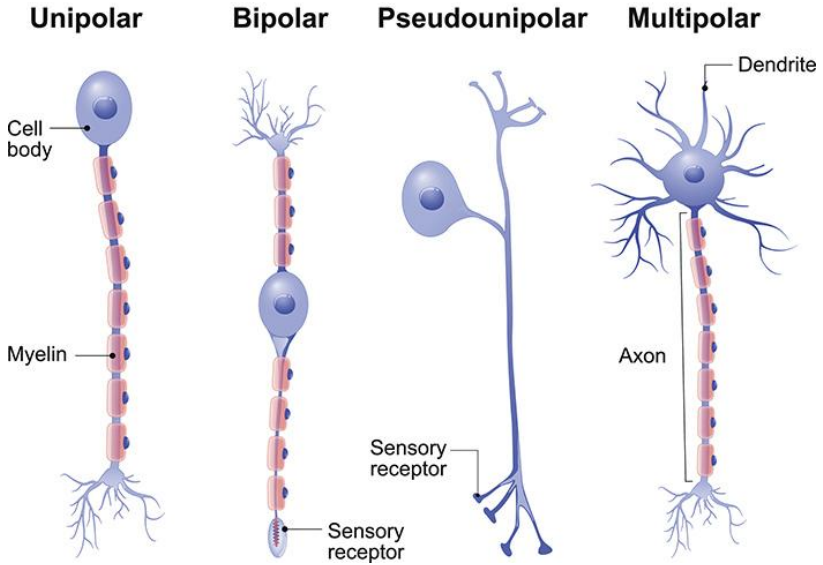
Brain Cell Diversity and Epigenetics

Dr. Mukamel

1. How do cell types within the CNS differ?

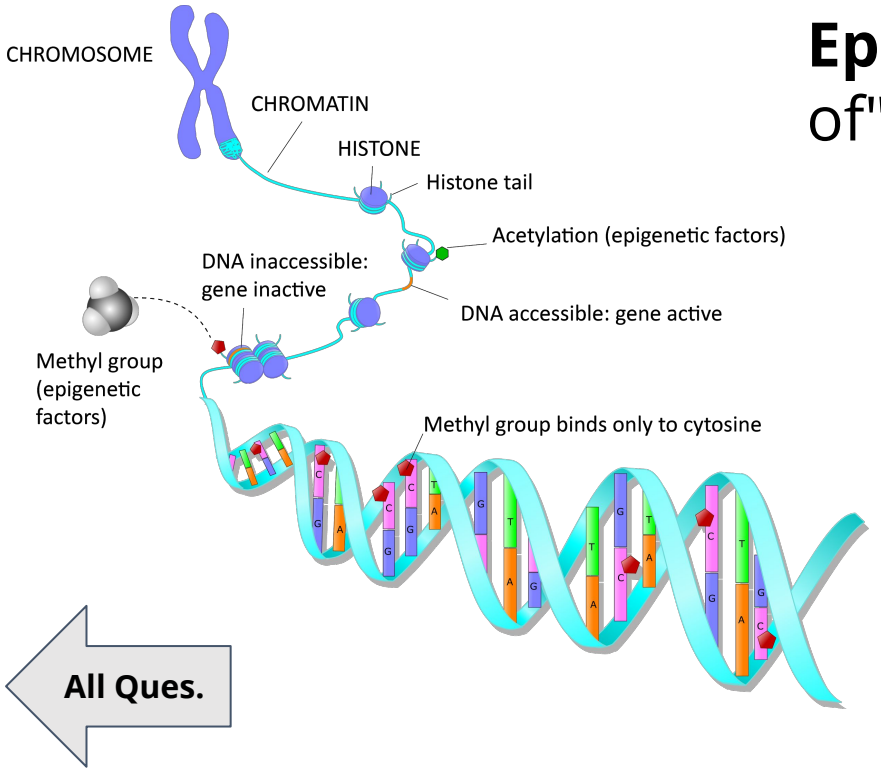
Categories of Differences:

- Location (area, layer)
- Connection (inputs / outputs)
- Electrical / chemical responses
  - Excitatory or inhibitory?
- Morphology



All Ques.

2. What is epigenetics?



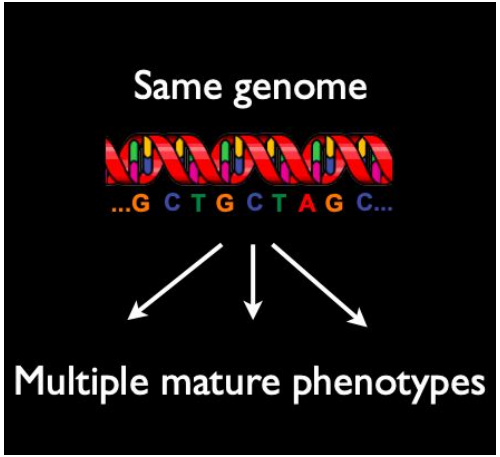
All Ques.

Epigenetics ⇒ "above" or "on top of" genetics (prefix “epi”)

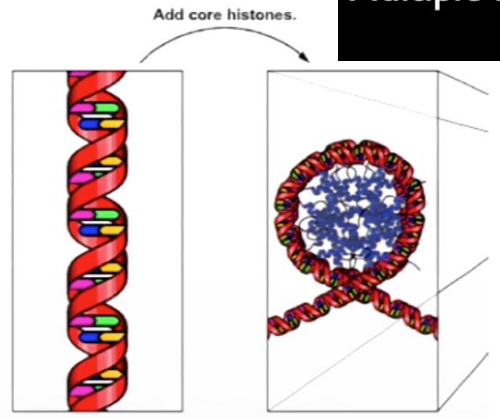
- External modifications to DNA ⇒ can turn genes "ON" or "OFF"
- Affect how cells "read" genes (**doesn’t change actual sequence**)

2.a/b How do cells become distinct despite having the same genome? What are histones?

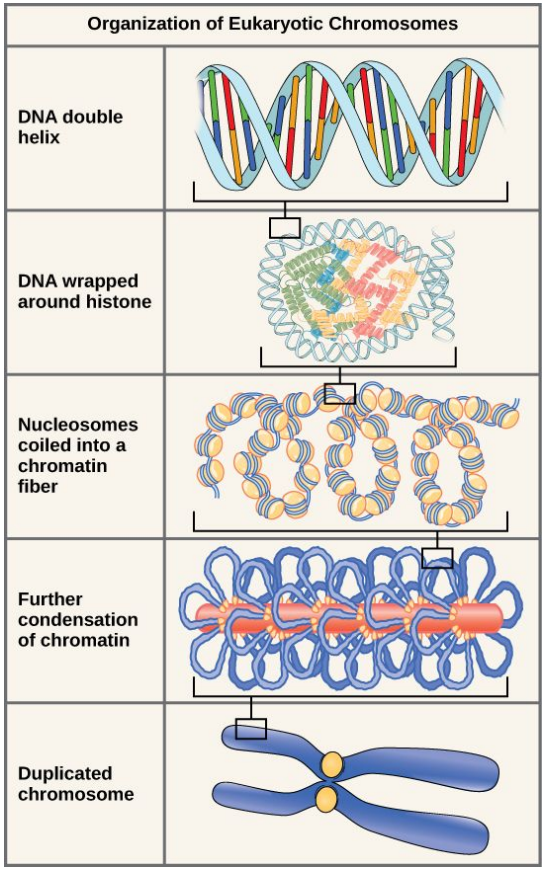
- Distinctive cells ⇒ <u>epigenetic modifications</u> to DNA.
- **Histones** = proteins that package / order DNA.
  - “Spools” around which DNA winds
  - Play a role in gene regulation



All Ques.



3. What are the basic levels of organization in the genome?



DNA

↓

Histones → **Nucleosome**

↓

Scaffold proteins (e.g. chromatin)

↓

Chromosome

All Ques.

4. How is epigenetics analogous with grammatical punctuation? What is DNA methylation and what is its function?

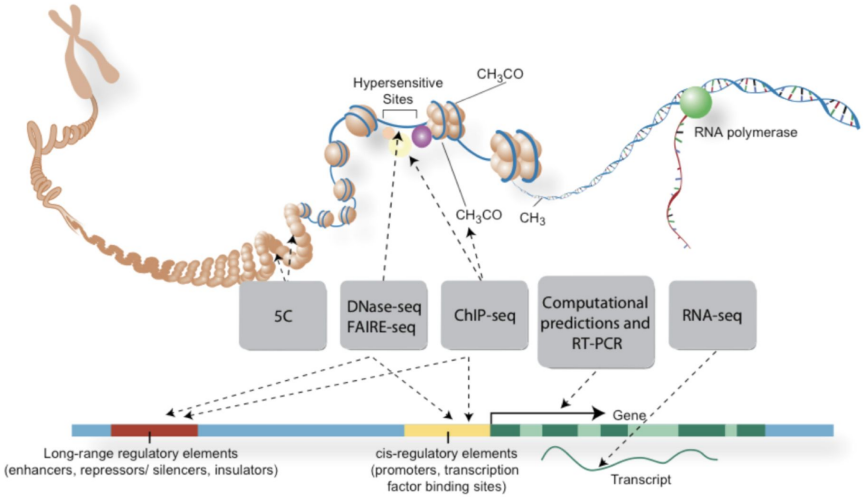
Epigenetics: Punctuation. Is. Key.

STOP CLUBBING BABY SEALS!!

STOP CLUBBING, BABY SEALS!

All Ques.

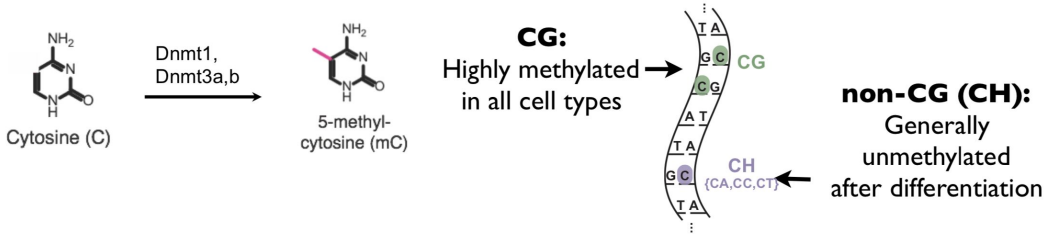
Modifications to DNA are epigenetic "punctuation marks"



Encyclopedia of DNA Elements (ENCODE) (2012)

4. How is epigenetics analogous with grammatical punctuation? What is DNA methylation and what is its function?

Cytosine DNA Methylation



- Covalent modification of genomic cytosine (mC)
- Key roles in imprinting, X-inactivation, transcription repression, cancer
- Stable and heritable
- Yet, reversible and potentially activity-dependent
- *Rett syndrome:* An autism-spectrum disorder caused by Methyl-C Binding Protein (MECP2) loss of function

All Ques.

5. How can methylation affect phenotype?

Maternal care induces life-long changes in DNA methylation and stress resilience in offspring

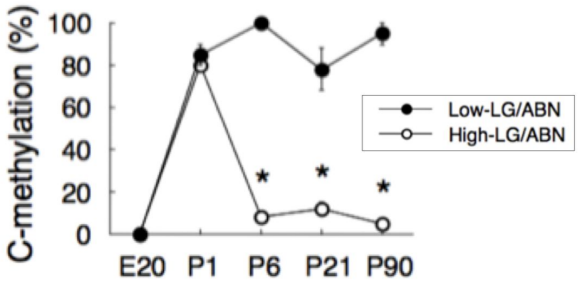
Low quality maternal care

↑ Stress behavior of offspring

↓ Glucocorticoid receptor (GR) expression in brain

High quality maternal care

GR promoter is hypermethylated in hippocampus in low-quality group [Weaver, …, Szyf, Meaney (2004)]



Maternal Care

↓

Offspring DNA methylation

↓

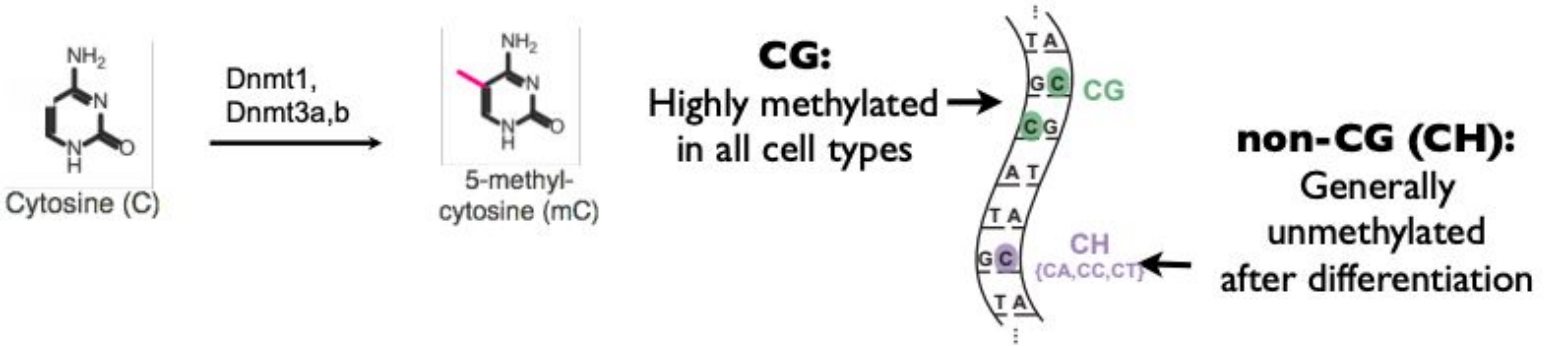
Offspring GR expression

↓

Offspring stress behavior

All Ques.

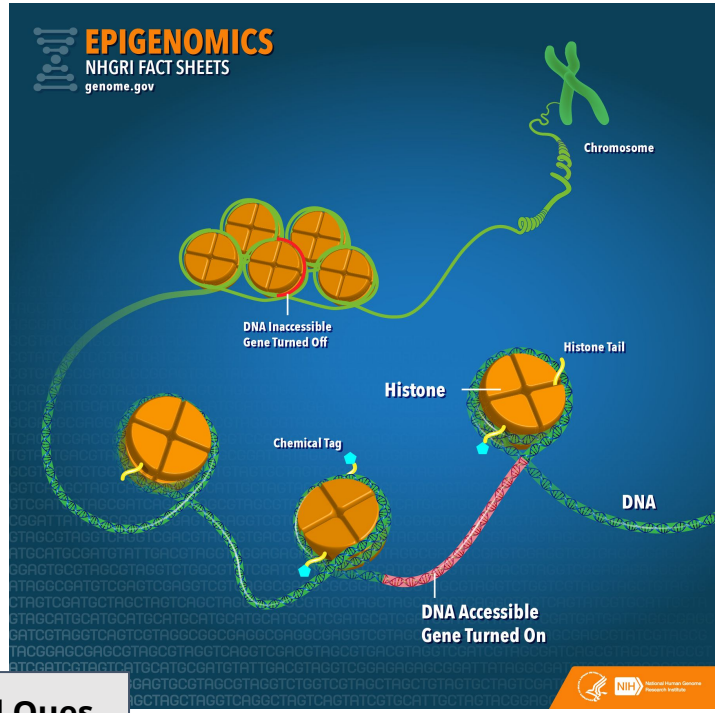
5. How can methylation affect phenotype?



- Covalent modification of genomic cytosine (mC)
- Key roles in imprinting, X-inactivation, transcription repression, cancer

All Ques.

6. Do epigenetics change over time? Or are they permanent? Why?



All Ques.

- Chemical modifications ⇒ alterations in gene expression
  - These are heritable
- <u>Examples</u>:
  - DNA methylation
  - Histone acetylation

7. What is shotgun sequencing?

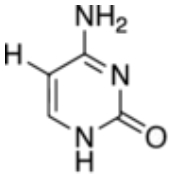
Measures the “DNA methylation landscape”
⇒ Way to study large, complex gene networks

1. Cut DNA into tiny fragments
2. Clone fragments
3. Use computational algorithm to reassemble sequence based on overlapping fragments

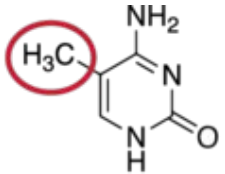
All Ques.

8. How do the levels of CG and non-CG methylation change throughout a human's life and in different cell types?

CG methylation	non-CG methylation
Highly methylated in all cell types	Generally unmethylated after differentiation
Stable & heritable	Substantial in (mature) neurons
Key roles in imprinting, X-inactivation, transcription repression & cancer	↑↑ during yrs 0-16 (w/ synaptogenesis & pruning



Cytosine

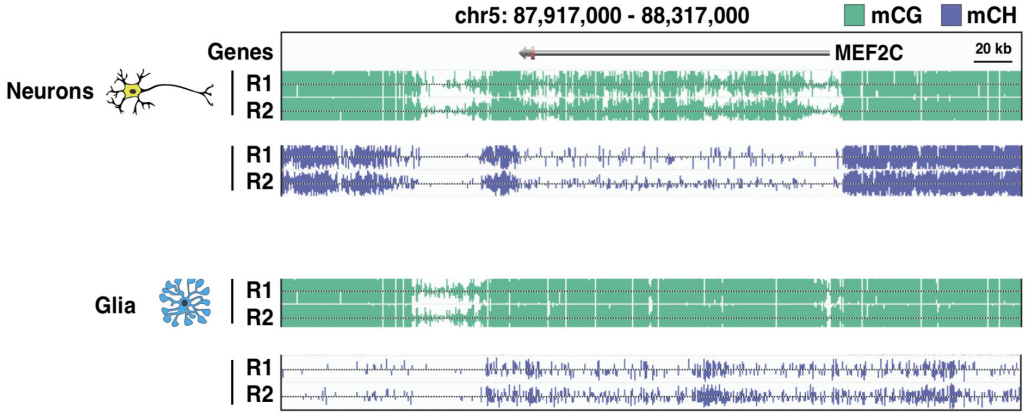


methylated Cytosine

All Ques.

8. How do the levels of CG and non-CG methylation change throughout a human's life and in different cell types?

Cell types have unique DNA methylation fingerprints



Transcription factor MEF2C:

- Implicated in neurogenesis and cortical development
- Hypermethylated (*i.e.,* repressed) in glia

All Ques.

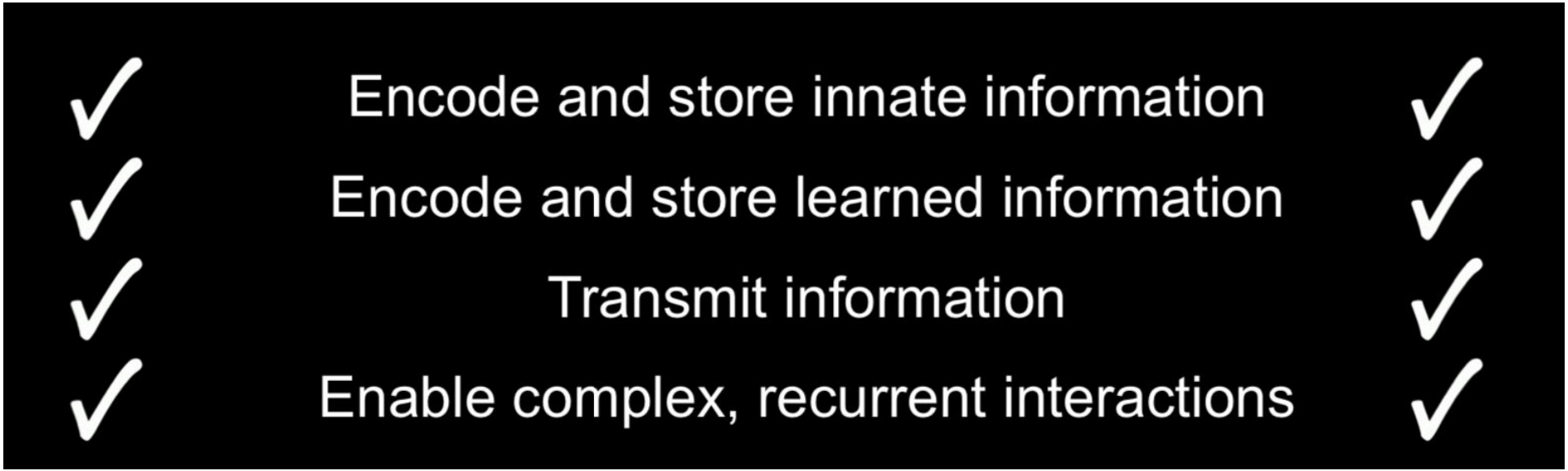
9. How do epigenetics play into the debate of nature vs. nurture?

Power of environment to affect methylation
⇒ e.g. maternal care & effects on stress resilience

Methylation patterns are strongly conserved between individuals

All Ques.

10. What are the similarities and differences between neural networks and gene networks?



All Ques.

Lecture 6

Neuronal Regeneration

Dr. Rangel

11. Is the number of neurons in our brain constant over lifetime?

Neurons in the Brain:

Roughly 80-120 billion neurons (estimate)

neurons ⇒ **constantly changing**

There can be:

- **Loss**
- **Gain**

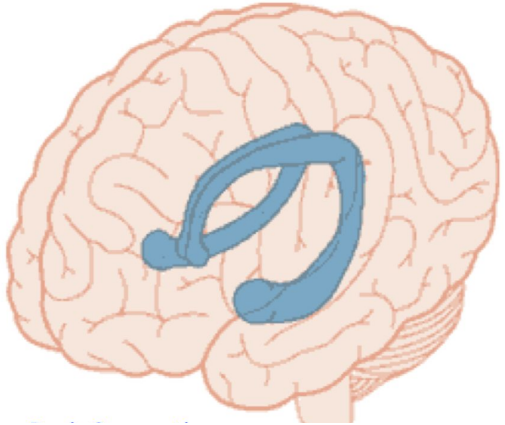
Can you give examples that might result in both?

All Ques.

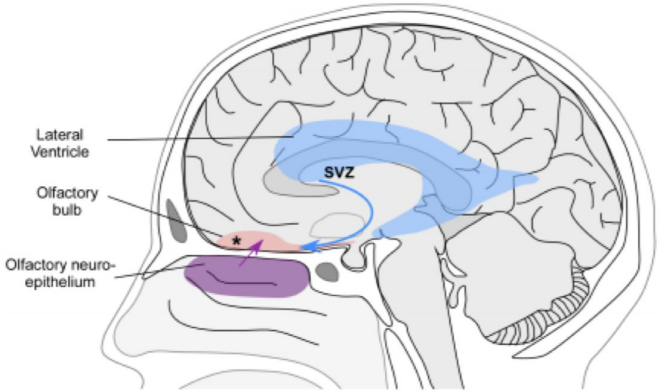
12. What are the two main neurogenic regions in human brain?

Two Main Neurogenic Regions:

The **subgranular zone** of the dentate gyrus:



The **subventricular zone** of the lateral ventricle:



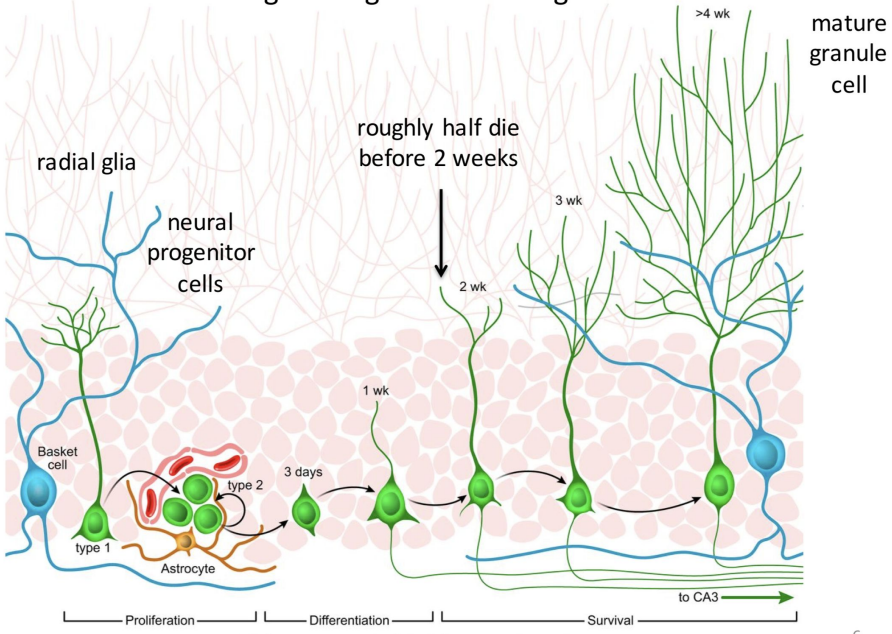
All Ques.

NOTE: the **dentate gyrus** is a sub-region of the **hippocampus**

13. What are the stages of new neuron development? What happens at each stage?

New neuron development:

from dividing radial glia to mature granule cell



This process is **highly regulated**

Aimone et al., 2014

All Ques.

Proliferation

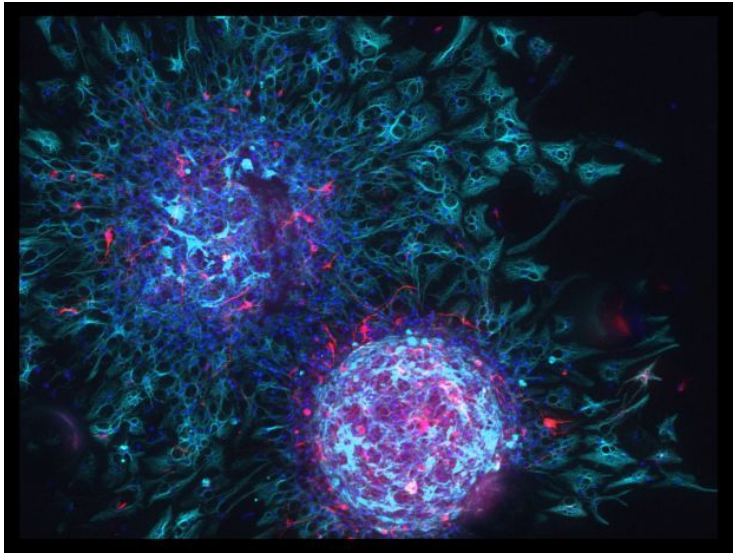
Differentiation

Survival

14. How can we quantify neuron proliferation and survival? (Doublecortin (DCX) and BrdU)

Measuring proliferation

- BrdU = thymidine analog incorporated into DNA of dividing cells during S-phase
- How many cells are dividing / or immature at time of measurement?



Measuring survival

- DCX = doublecortin (MAP expressed in first 2-3 weeks)
- How many newborn cells survive?

All Ques.

15. What are some factors that can affect the proliferation/survival rate of neurons? Does increase in neuron proliferation also mean increase in neuron survival?

Proliferation	Survival
Stress ↓	Learning ↑
Physical exercise ↑	Alcohol ↓
Antidepressants ↑	Dietary restriction ↑
Aging ↓	Enriching environments ↑
Seizures ↑	

KEY POINT:
Proliferation ≠ survival!

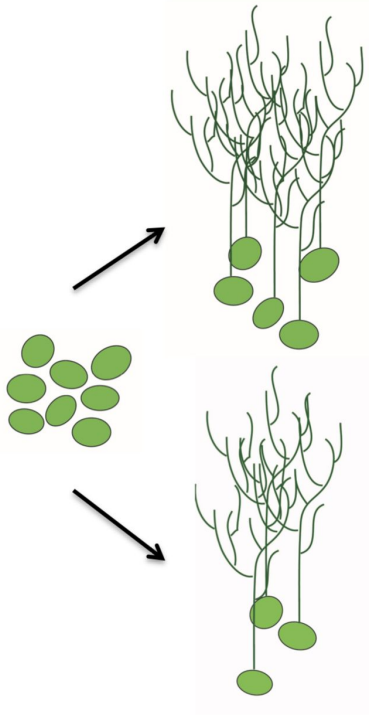
All Ques.

15. a. Does increase in neuron proliferation also mean increase in neuron survival?

Many things can influence adult neurogenesis

survival is highly regulated

- Adult neurogenesis can be regulated at different stages of neuron development.
- Increased proliferation does not necessarily mean that there are more that survive.
- The fact that this process is highly regulated suggests that these cells may serve a special function.



All Ques.

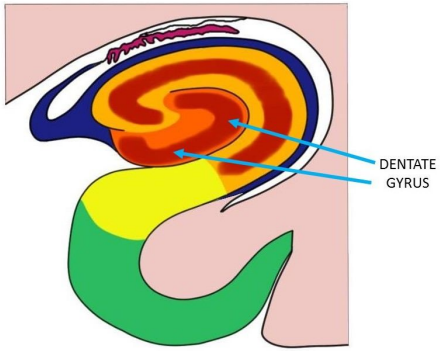
16. What are the major functions of the hippocampus and dentate gyrus?

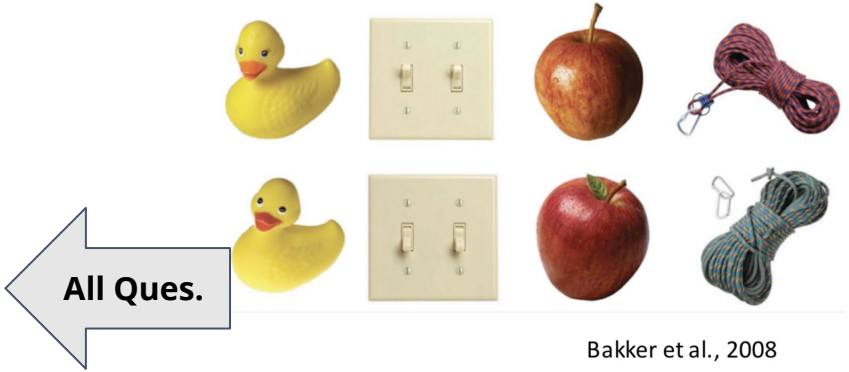
Hippocampus

- Critical structure for learning & memory

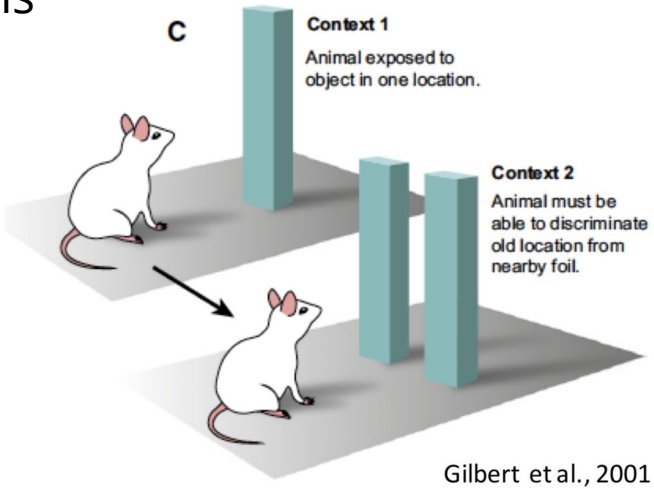
Dentate gyrus

- Sub-structure of hippocampus
- Important for fine discrimination between similar experiences / objects &/or spatial locations



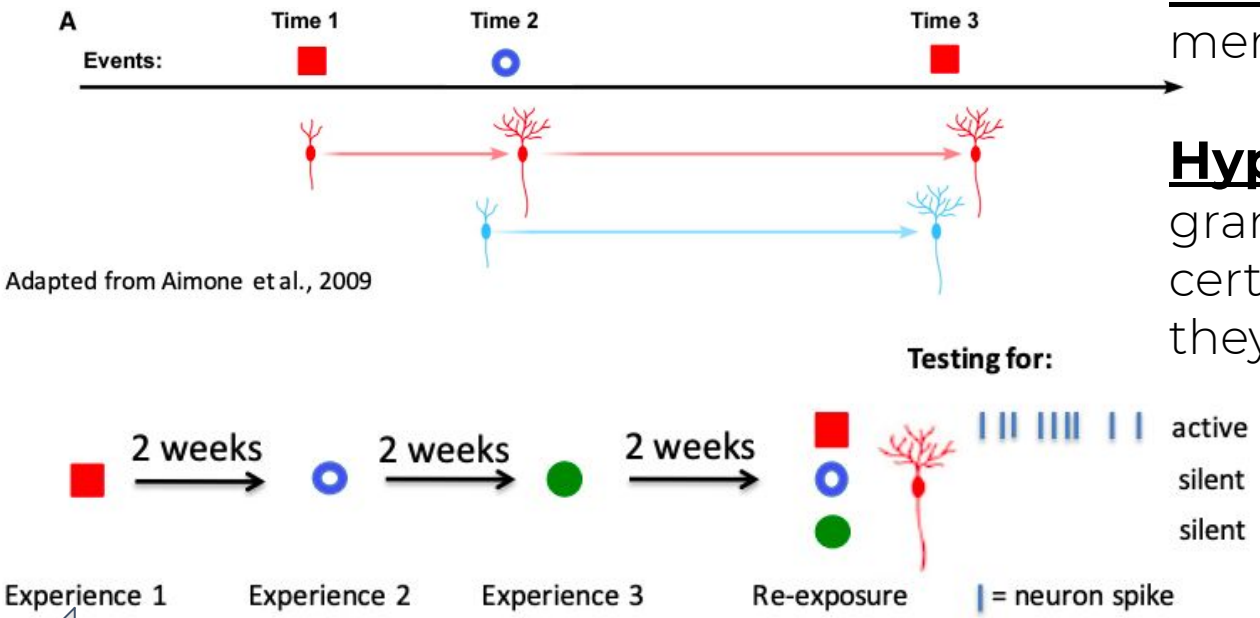


Bakker et al., 2008



Gilbert et al., 2001

17. What is a hypothesized function of young cells in the hippocampus? How do the experiments described in lecture support this hypothesis?



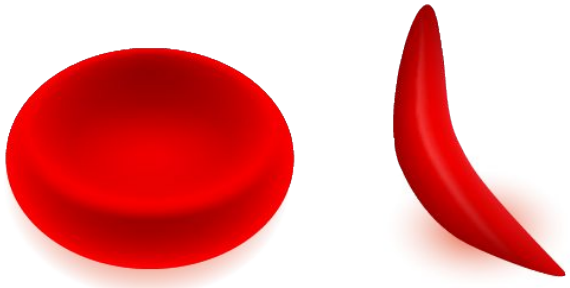
Recall: hippocampus ~ memory

Hypothesis: Activity of granule cells ⇒ selective for certain experiences (i.e. when they were developing)?

What is this showing?

All Ques.

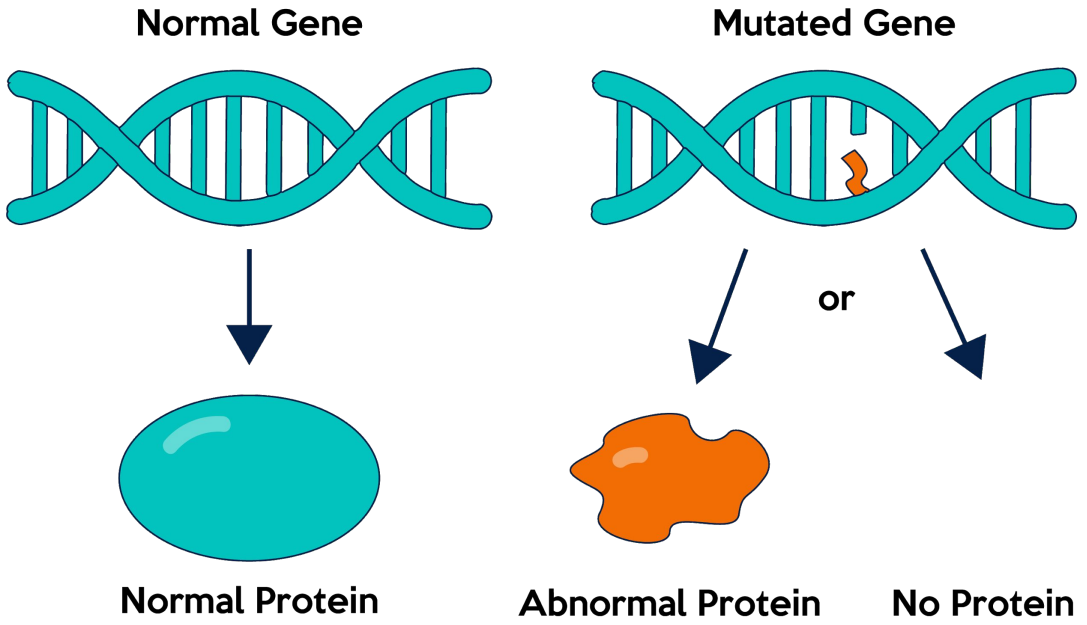
18. What are some negative effects of gene mutations?



Normal red blood cell

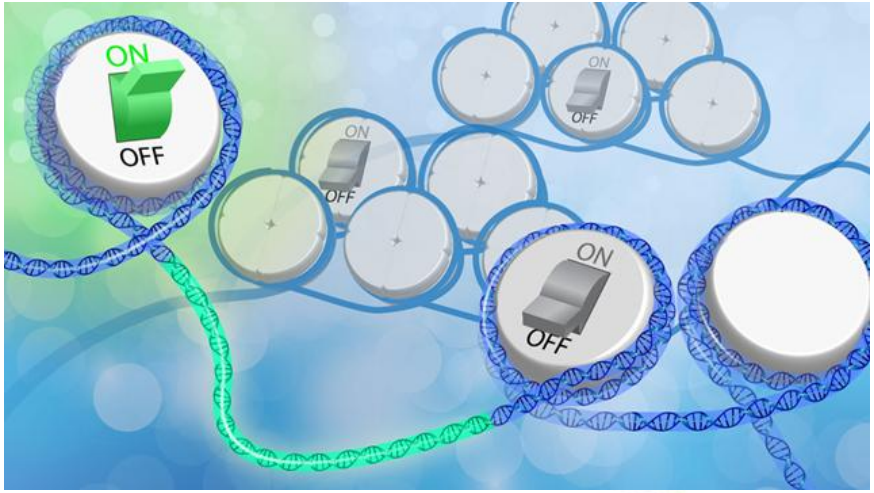
Sickle cell

Abnormal proteins ⇒ disease
(e.g. sickle cell anemia)

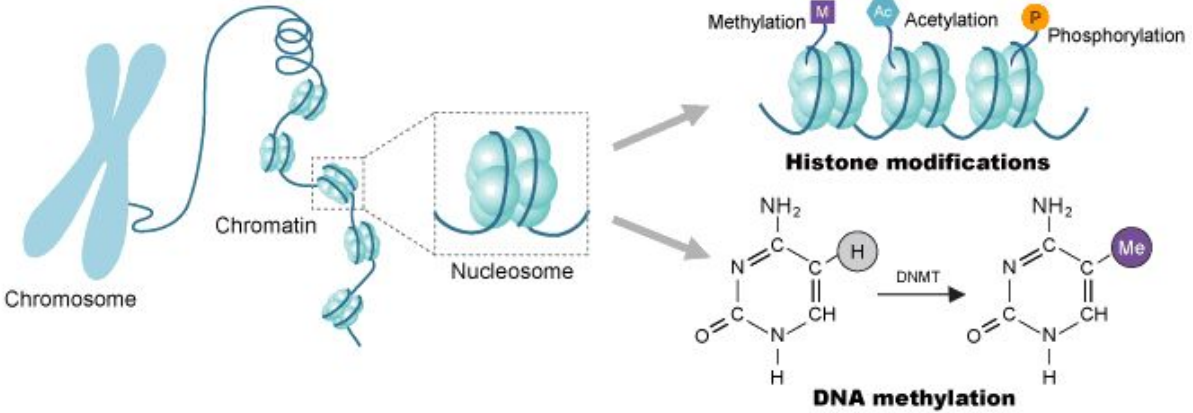


All Ques.

19. What does the field of epigenetics concentrate on?

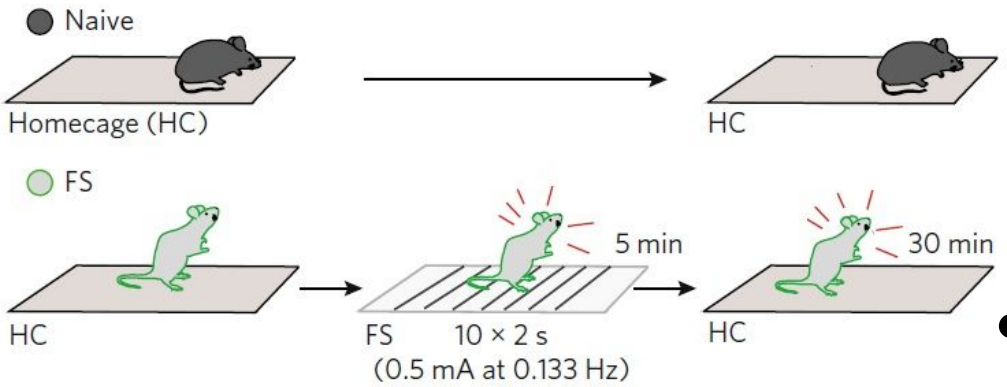


Focus on: **modifications**
Less emphasis on: changes to actual code



All Ques.

20. How did experimenters make the parent mice afraid of certain smells? What effects does this have on the parent mice and their offspring?



- Pair an fruity odor w/ mild foot shock ⇒ <u>condition fear</u>
  - Odor ⇒ change to organization of neurons in olfactory bulb
- F1 generation ⇒ **<u>increased startle</u>** <u>to odor</u> *even w/o prior exposure!*

All Ques.

21. What can be said about famine and disease? (from the reading → “Tales of Adversity”)

Dutch Hongerwinter (1940s) & Great Chinese Famine (1950s)

⇒ There is a <u>trans-generational relationship</u> between **food** and **genes**

Children wait to be fed during the Dutch Hongerwinter of 1944–1945.

All Ques.

22. Give examples of epigenetic changes and how they affect risk of disease.

Children wait to be fed during the Dutch Hongerwinter of 1944–1945.

All Ques.

Link methylation of IGF2 to

- ↓↓ methylation of IGF2 should ↑↑ expression of the hormone

Nearly six decades after the famine, Lumey and colleagues isolated DNA from Hongerwinter individuals. They found a below-average methylation of the insulin-like growth factor II gene *(IGF2)*, which codes for a growth hormone critical to gestation. Decreasing the methylation of *IGF2* should increase the expression of the hormone. In contrast, later studies in this cohort found increased methylation of five other genes, among them genes associated with cholesterol transport and ageing, as well as the gene that produces IL-10, which has been linked with schizophrenia.

Quiz Time!

- No talking, signaling, or communicating of any kind.
- Put away your books, notes, computers, phones, etc.
- Pen or pencil is okay (just make sure it's a black pen and you press hard with a pencil).
- Write your name in the "Name" box, write and circle in your PID, and sign the academic integrity agreement.
- Bubble in this section
- Please have your student ID out when you turn in your quiz!

Write and circle in your PID

Write down your name here

UC SAN DIEGO – DEPARTME OF COGNITIVE SCIENCE

STUDENT PID NUMBER								
A/U								
[0]	0	0	0	0	0	0	0	0
[1]	1	1	1	1	1	1	1	1
[2]	2	2	2	2	2	2	2	2
[3]	3	3	3	3	3	3	3	3
[4]	4	4	4	4	4	4	4	4
[5]	5	5	5	5	5	5	5	5
[6]	6	6	6	6	6	6	6	6
[7]	7	7	7	7	7	7	7	7
[8]	8	8	8	8	8	8	8	8
[9]	9	9	9	9	9	9	9	9

Last NAME, First NAME
COURSE NUMBER
COGS 1
SPRING 2019
Dr. Mary ET Boyle
Quiz A
April 9-12, 2019
Quiz VERSION

A	B	C	D	E	F	G	H
■	B	C	D	E	F	G	H

Section you are taking this quiz:
Please Bubble only one!
[1] 1 Monday @ 9 Lexi D.
[2] 2 Monday @ 4 Elena
[3] 3 Wednesday @ 2 Adrian
[4] 4 Wednesday @ 3 Audrey
[5] 5 Wednesday @ 5 Devansh
[6] 6 Friday @ 11 Lori
[7] 7 Friday @ 12 Elena
[8] 8 Friday @ 1 Lexi F.

Bubble in the current section

Quiz will not be graded without Academic Integrity Signature.

ACADEMIC INTEGRITY

By taking this quiz, you agree that you will follow ALL UCSD ACADEMIC INTEGRITY policies.
It is YOUR responsibility to know and understand all of the policies.
Failure to follow all UCSD Academic Integrity policies could result in expulsion from UCSD.
DO NOT DISCUSS THIS QUIZ CONTENTS WITH FELLOW STUDENTS!!!

Signature Date

Your **signature above certifies** that you *will follow* and that you know that you will suffer the consequence for ANY academic integrity violation.

Sign and date here

YOUR ANSWERS GO HERE

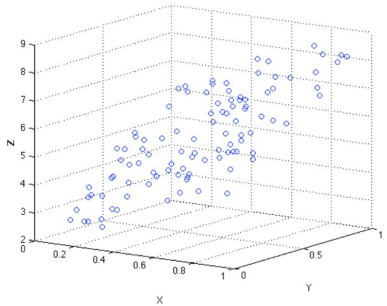
	[A]	[B]	[C]	[D]	[E]
1	A	B	C	D	E
2	A	B	C	D	E
3	A	B	C	D	E
4	A	B	C	D	E
5	A	B	C	D	E
6	A	B	C	D	E
7	A	B	C	D	E
8	A	B	C	D	E
9	A	B	C	D	E

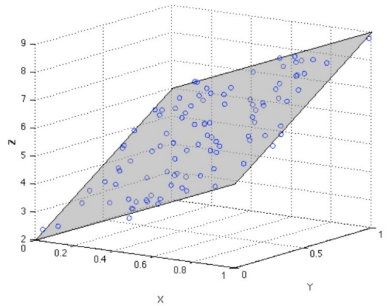
Bubble in the answers

Describe Principal Components Analysis (PCA). What is it? How is it utilized in studies investigating gene expression? What are some limitations?

Dimensionality reduction by Principal Components Analysis (PCA)

- Principal components analysis (PCA) projects high-dimensional data onto a smaller number of “most interesting” dimensions

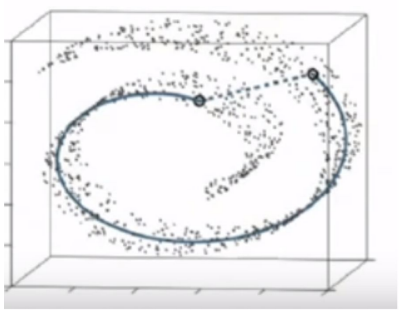


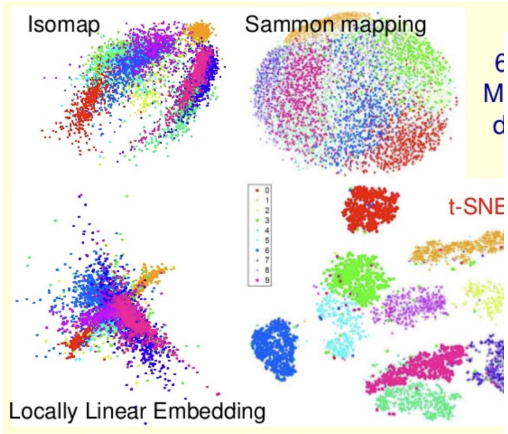


All Ques.

What is tSNE? What are some advantages of using this method?

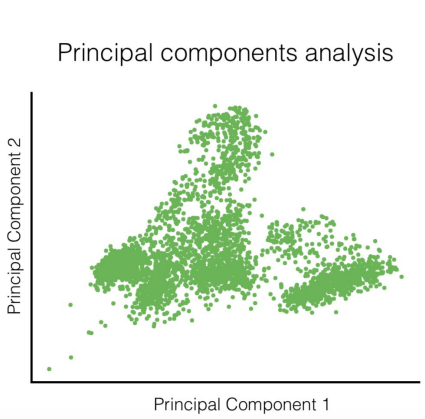
tSNE (t-Stochastic Neighbor Embedding)
Visualizing cells in a high-dimensional space

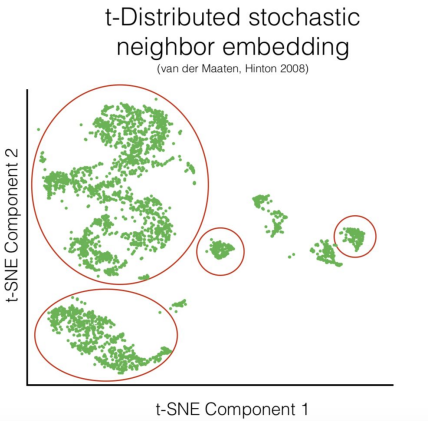




All Ques.

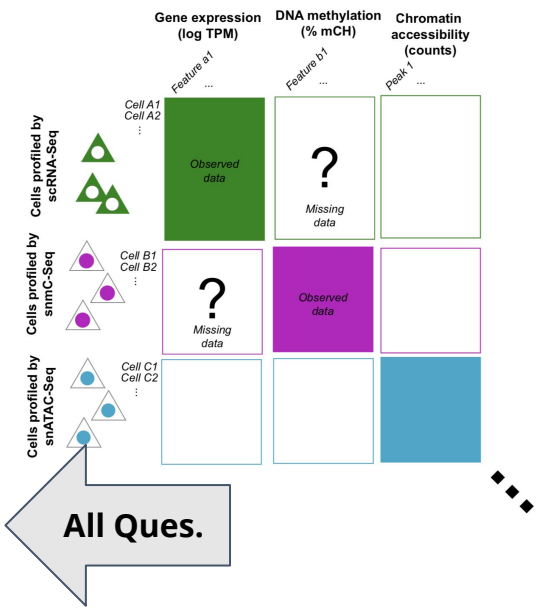
Linear and non-linear dimensional reduction

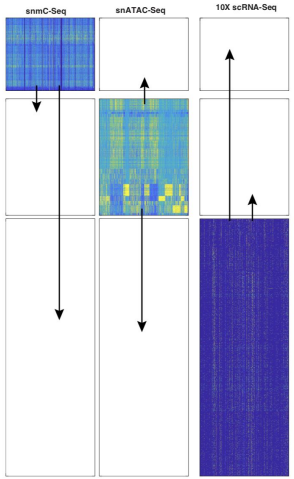




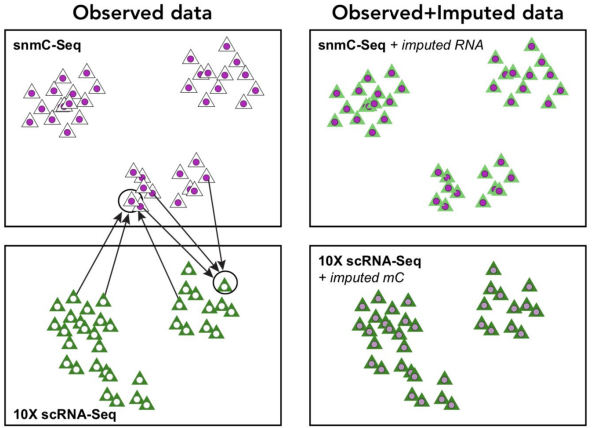
What is the goal of data imputation in DNA sequencing and analysis?

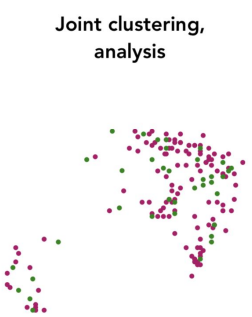
Multi-omics data integration requires imputation





Cross-modality data fusion by *Bigraph Imputation*

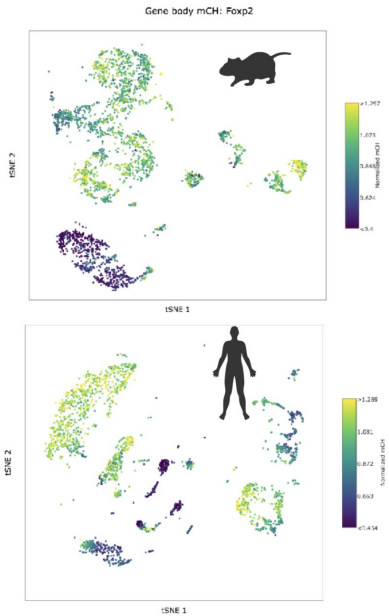


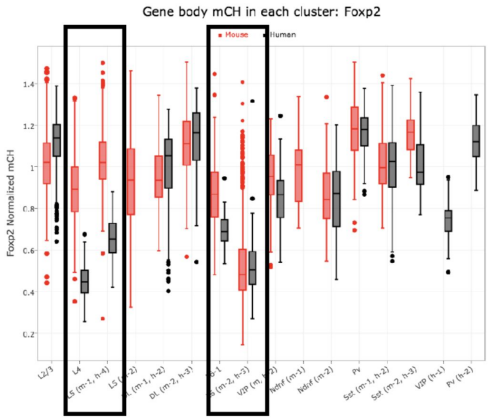


- For each cell in modality A, find K neighbors in modality B
- This requires a *linking assumption*, e.g. low gene body mCH corresponds with high mRNA expression
- Use neighbors to impute missing information for A

What is the significance of the FOXP2 gene, as discussed in lecture?

FOXP2 (associated with language) is expressed in different cortical layers in mouse and human frontal cortex





All Ques.

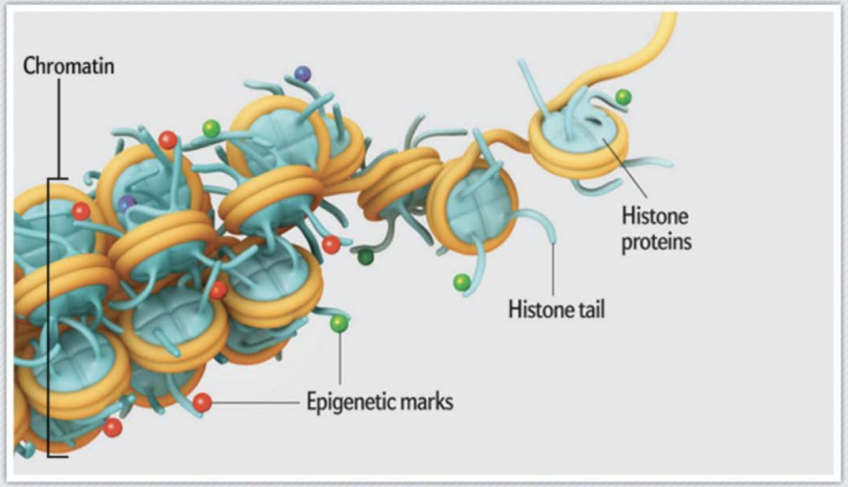
How do epigenetic marks affect genes? At which locations do they occur? Are they permanent?

- Epigenetic marks can turn off genes (DNA Methylation) or turn them off (Acetylation)
- They are chemically stable and heritable

All Ques.

3. What Epigenetic Marks Are

The DNA in our cells is wrapped around complexes of proteins called histones, like thread around a spool; the combination of DNA and histone protein is known as chromatin. Epigenetic marks are chemical groups of various sorts that decorate the histones and DNA; they can be added or subtracted in response to environmental factors and experience.



Next »

Are changes observed in offspring socially transmitted or inherited? How did researchers account for this?

Text

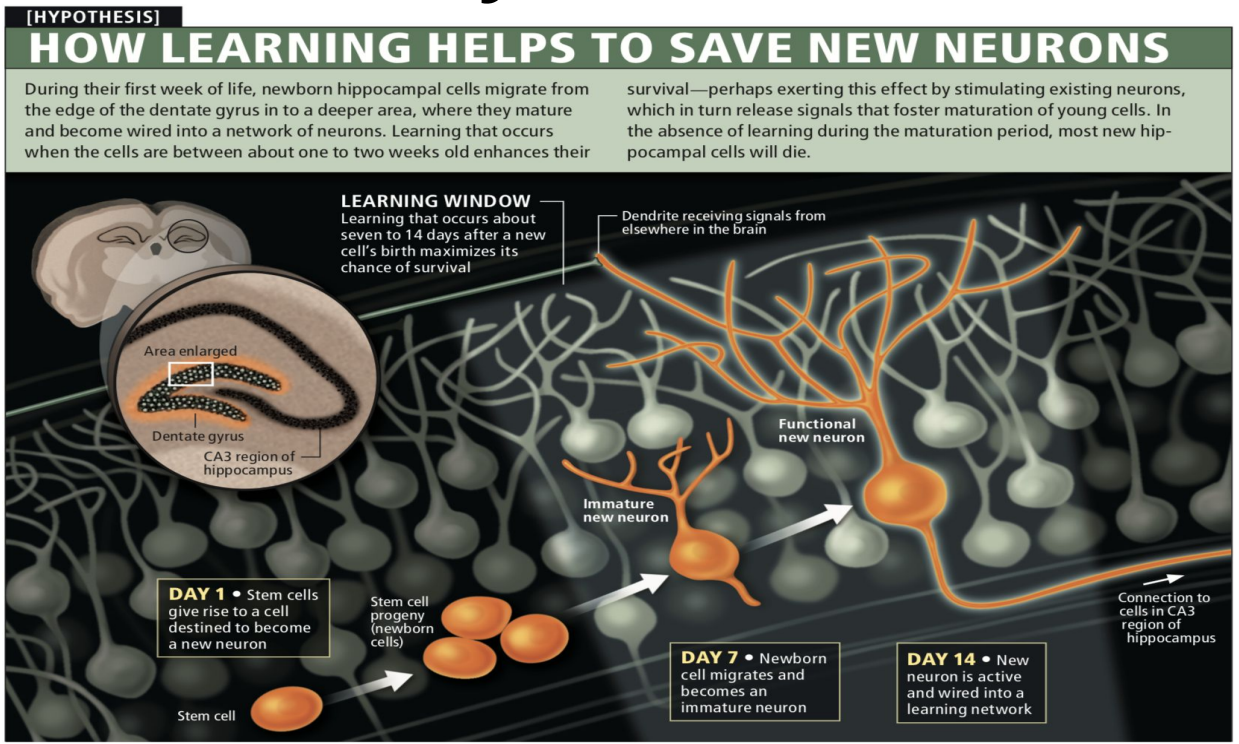
All Ques.

Are the memories being passed down fear or sensitivity? Why or why not? What role do epigenetics play in this process?

Text

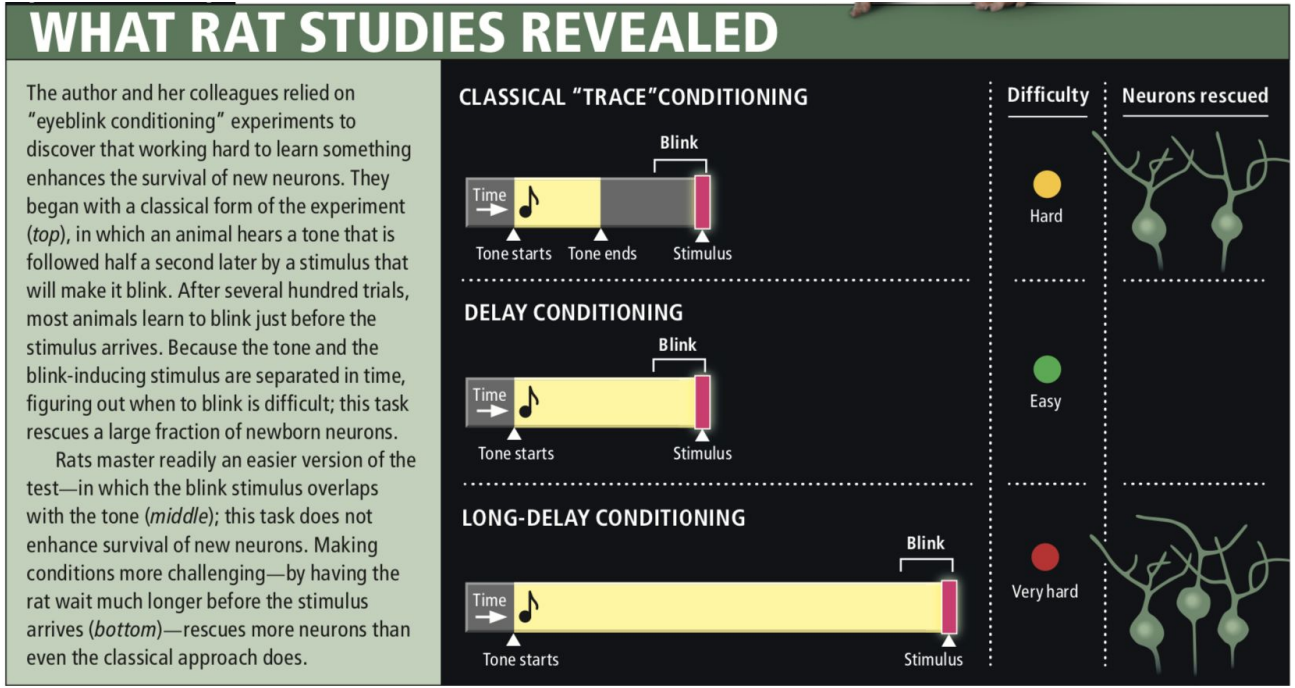
All Ques.

How does learning enhance survival of new neurons in the adult brain? What are the limitations of its ability?



All Ques.

Know the rationale behind the animal experiments introduced in the reading. Understand the experiment designs and results.



All Ques.