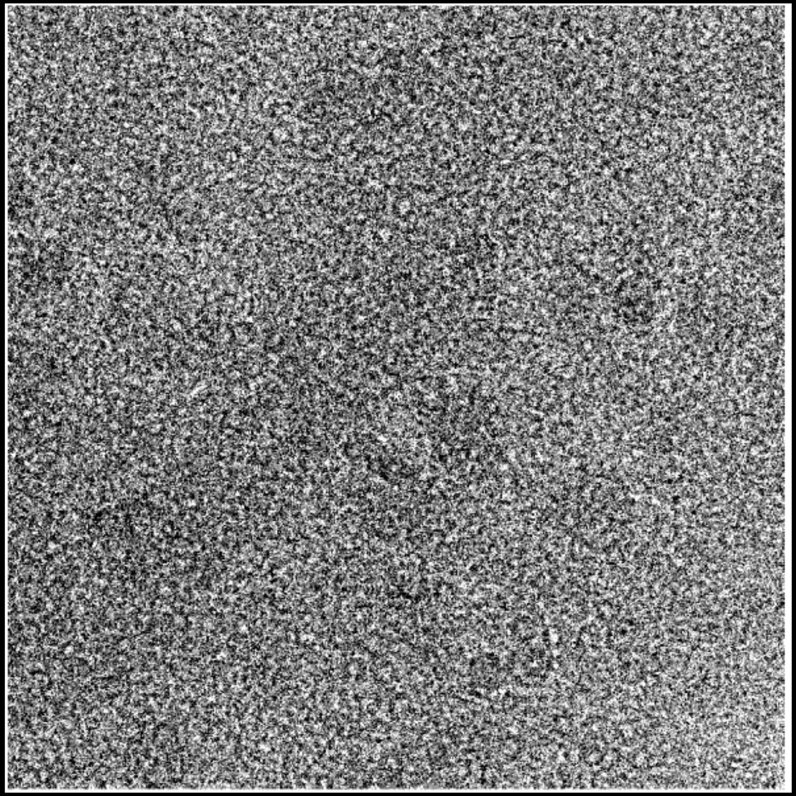
Vs
BCBMB

Simple Question: What do you see?

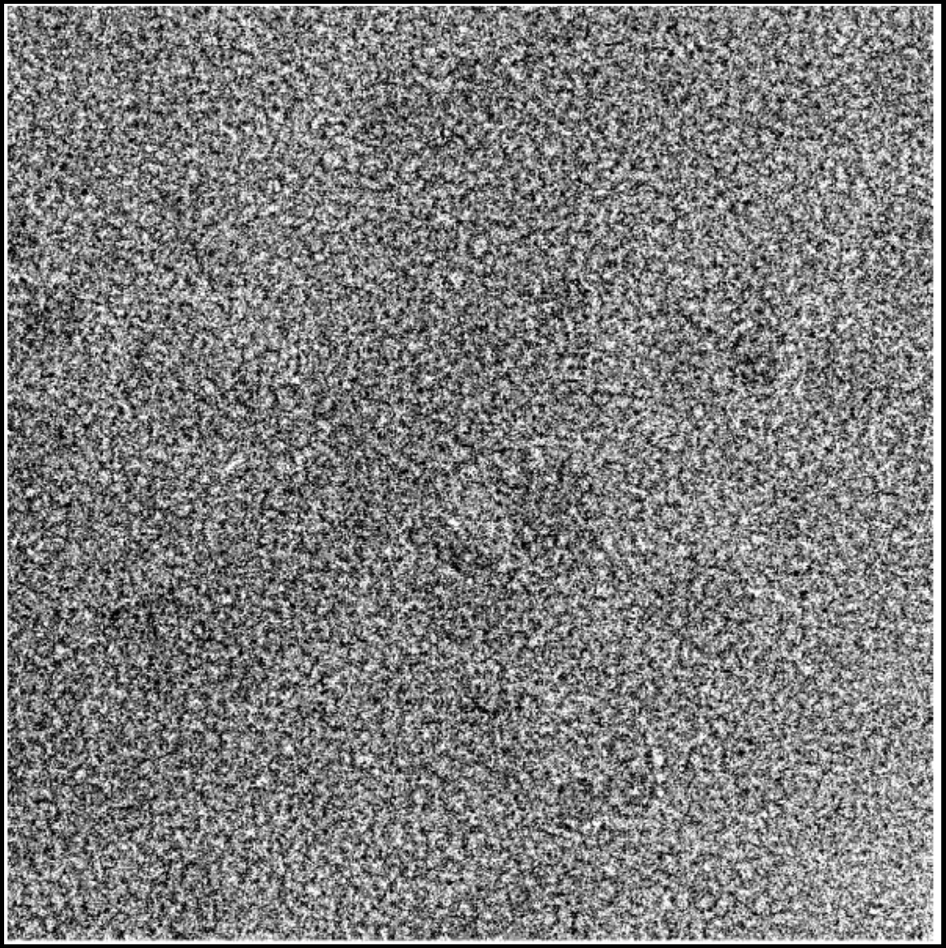
… if you answered Earth …. then try this one…. what do you see here?



Noise? A bad screen saver/slide background?

If you are at a loss with this one….good …because "being lost here" lets you understand why "Earth" was **not** the answer for the previous image … **HOW SO?**

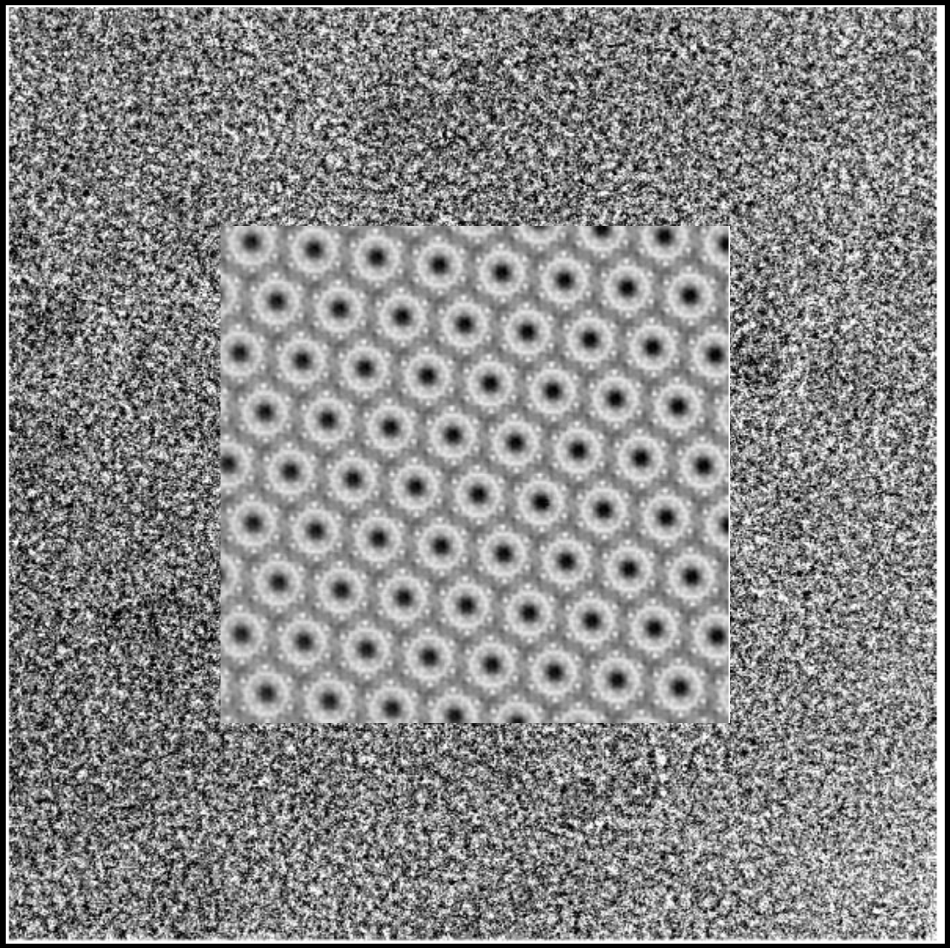
If "Earth" had been the appropriate answer, then in this case, an equivalent answer would be



unprocessed cryogenic image of
a 2D-gap junction array

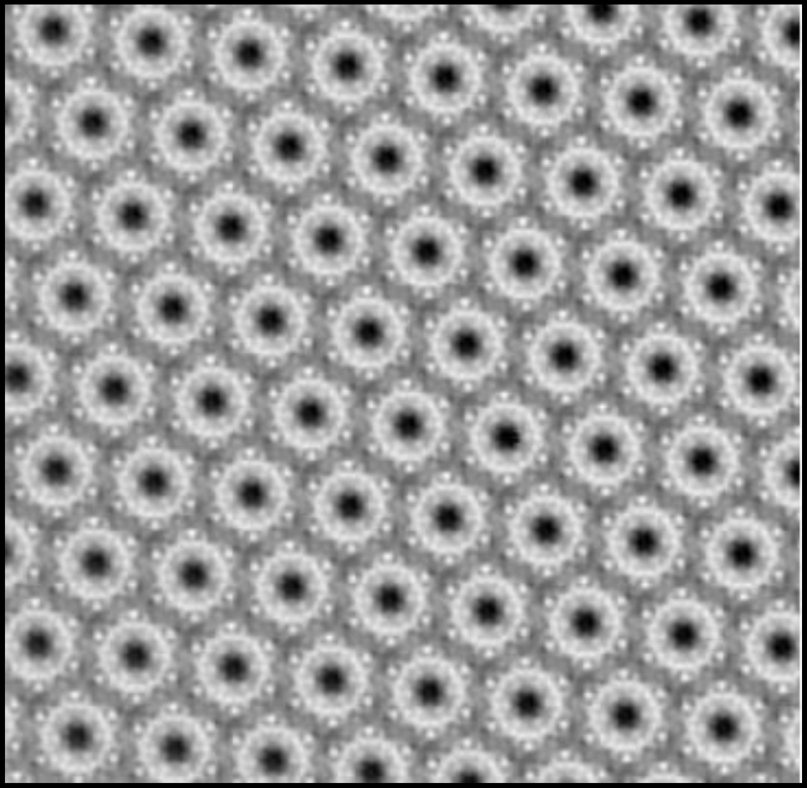
?!!???

"unprocessed": cryogenic images are very noisy (and that is part of what you see/"feel") … but fortunately, one can "clean" them up by digital image processing ……



the insert in the centre shows how the fully processed and corrected image looks like …. magic …. :) (if you want to know more about how this is done … reach out and we can take a look)

But … even if I had shown you the fully processed image …and asked : "What Do You See?" …..



…..would you have said "a gap junction array" ?

VERY unlikely …. and THAT brings us to the **key issue**:

"Earth"?

…. does not answer what you see

…but **states your <u>correct interpretation</u> of what you see**

HOW is this relevant, and WHY should you care??
Let's answer those questions next….!

First Stop: what does asking "What Do You See" mean?

→ It is an **explicit** instruction to verbally describe and to "collect observational data"

Skill Set: Observing - Describing

Colors:
black, blue, green, brown, white

Objects (…this is taken to an extreme)

- Overall circular shape on square black background
- Circular shape has a smooth gradient of brightness from left to right
- Smooth and mostly featureless, interconnected blue regions that cover ~30% of the circular object and are more abundant than any other feature contained within the circular boundary
- Intermixed with the blue are irregular shaped and irregularly patterned white features that account for ~30% of the total circular area; there also is a less patterned, irregular shaped white region at the top center occupying ~5% of the total area of the circular area
- A bipartite, irregularly shaped feature - roughly aligning along a 11AM-5PM line – accounts for ~30% of the circular area. This feature has a complex pattern of interconnected brown and green territories. An additional small feature, mostly green colored, is observed roughly aligned with the 9AM-3PM line and to the right…...

What Don't you See?
Black part seems to be completely featureless.

Point to make here: accurately **DESCRIBING** observations **WITHOUT** getting mixed up in **INTERPRETATIONS** is harder than it sounds, **but** really important.

[…and … it's "cool" because you can describe something even if you do not have the slightest idea of what it may mean (like the weird second image I showed to you) = here you may start seeing the beginning of "relevance"]

Earth

Interpretations arise from correlating observations with prior knowledge. That is where it gets tricky because any description itself is based on knowledge. So where to draw the line?

Suggestion: even if you are >99% sure that you are right or truly “know” something, try to step back, and start “from scratch” by describing data in fundamental terms that minimize assumptions/bias/dogma/paradigm.

For instance:

- If you said Earth = true because you see North America and know it to be that → knowing that this shows Earth, you can readily identify other things like……scattered cloud patterns…..oceans....
- Here is where you may run into troubles: “white = clouds” ➔ not true because looking closely you will see the arctic ice sheet - also white – but hardly a cloud.

Similarly: this image is 2D → technically, you don’t see directly how the different colored objects relate in 3D. For all you know, they could be in a single plane [which you know to be wrong (eg the “artic and “clouds” are nowhere close each other spatially)]. Though: the "daylight → night" gradient suggests that Earth is a sphere → interpreting what you see retrieves some "3D info".

Another example for where things can get "iffy": the “black” background seems featureless compared to everything else ➔ technically, you should conclude that there is “nothing” ....but there is ...dark energy/matter for instance (check back in the "Cell Bio Intro Lecture").....and if the exposure were adjusted, you may see other stars looming in the background.

Agreed: this example **is** trivial and extreme. However, if this were “discovery science“ (where you do not already know the answers), then mixing/equating "interpretations" with "observations" will spell doom for your research, reading assignments and/or exams.

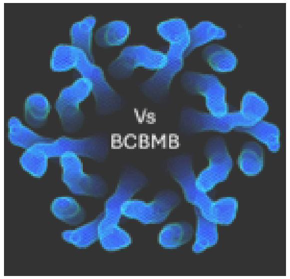
"Not looking closely & not being able to properly describe things in front of you without jumping to conclusions" is what we will call "**DATA BLINDNESS**".....

...working with students for >20 years, almost all of them WERE data blind .... not because they were born that way but because nobody ever told them & gave help to fix it (which is easy once you know what to do)

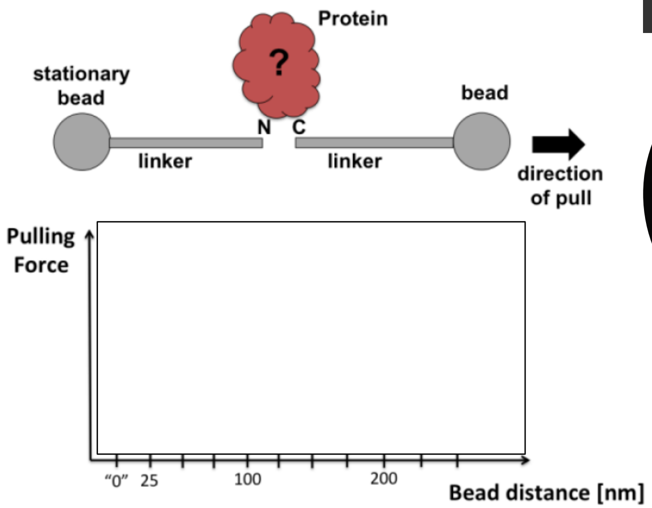
...even more scary: most students graduate without "fixing" data blindess (especially in STEM where multipe choice exams allow students to stay unaware) and that is a REAL problem ... for the students (and mankind alike)

...to help you see that I don't try to be just "mean" ... here is a "**REAL LIFE EXAMPLE**" where data blindness caught up with my students in a context that – in the bigger picture – is rather benign/inconsequential: **EXAMS**

Observing – Describing: Real Life Rationale



TASK 3
The picture shows you the general idea of an approach to study questions related to protein folding. Specifically: a rigid linker molecule is used to attach the N-terminus (N) of the protein to a stationary bead (left), while a second rigid linker molecule attaches the C-terminus (C) to a bead whose position can be manipulated and monitored (right). One type of experiment that is carried out with such a setup is to pull on the movable bead while watching how its position changes with respect to the other bead as the force of the pull increases. A potential outcome of such an experiment – plotting pulling force vs distance of the two beads – is shown in the lower part of the figure.

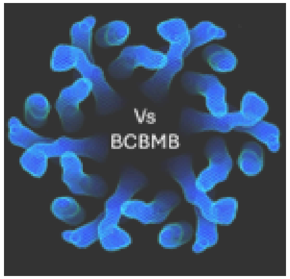


(a) Look at the data and <u>describe what</u> you see **(up to 2 points)**

Here are a few of the answers I got from students (none of them first years) in this exam. Based on these answers: draw a SKETCH of the function that goes into the force-distance panel above.

- **the force goes up and down as bead distance increases.**
- **looking at the data, it appears that the pulling force with respect to bead distance has a general positive treat. However, the pulling force drops occasionally before the pulling force starts to increase again. The distance between consecutive peaks is also increasing as the number of drops in pulling force occurs.**
- **As the pull on the bead to the right increases, the force needed to pull generally increases. However, it reduces sharply at some points (50, 100, 200), the peaks are also at these distances**
- **The data show that the pulling force has sharp decreases approximately at multiples of 50 nm (50 nm, 100 nm, 200 nm) and increases smoothly and gradually in the interim.**

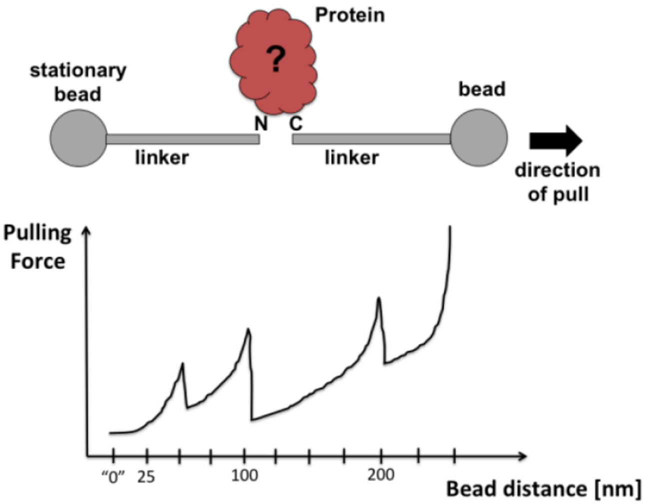
Observing – Describing: Real Life Rationale



Did you come up with the curve that is now shown, and was shown to the students asking them to describe what they see?

Doing this with my students for over 10 years, none ever did = if you didn't get it right – you are not alone!

TASK 3
The picture shows you the general idea of an approach to study questions related to protein folding. Specifically: a rigid linker molecule is used to attach the N-terminus (N) of the protein to a stationary bead (left), while a second rigid linker molecule attaches the C-terminus (C) to a bead whose position can be manipulated and monitored (right). One type of experiment that is carried out with such a setup is to pull on the movable bead while watching how its position changes with respect to the other bead as the force of the pull increases. A potential outcome of such an experiment – plotting pulling force vs distance of the two beads – is shown in the lower part of the figure.



(a) Look at the data and describe what you see **(up to 2 points)**

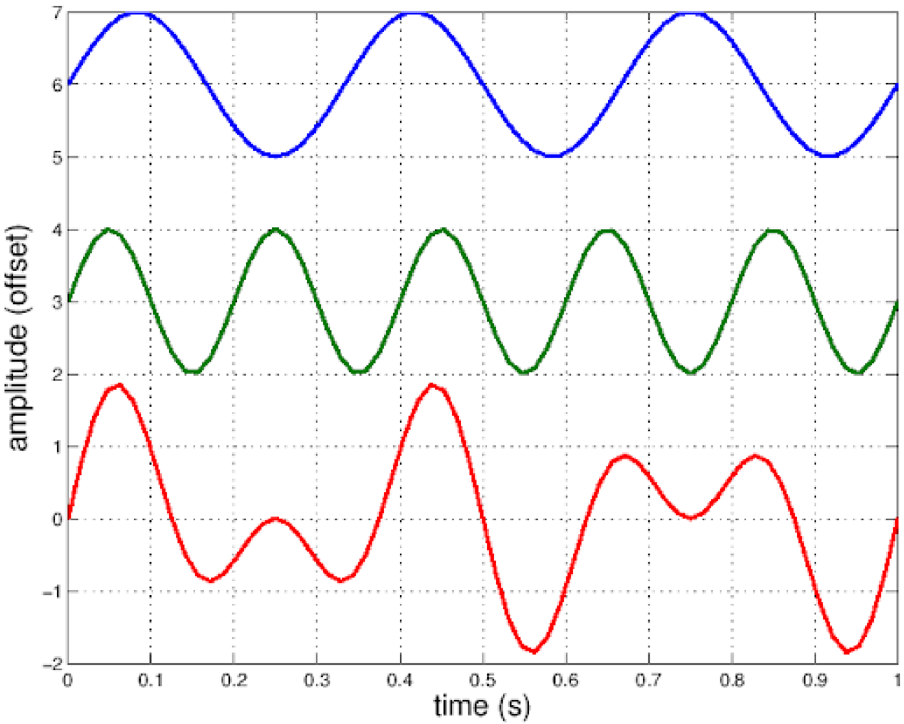
With all of what we went over so far – test yourself by trying to describe what you see; what if anything would you do differently/add to the description?

If you are unsure how to do this "properly", then continue … because from here on out, explicit examples will be used to "train" your eye to look/discover the things that are relevant.

Vs
BCBMB

Observing – Describing: Warm-Up

Write down a bullet list of **observations** (= "what do you see?)



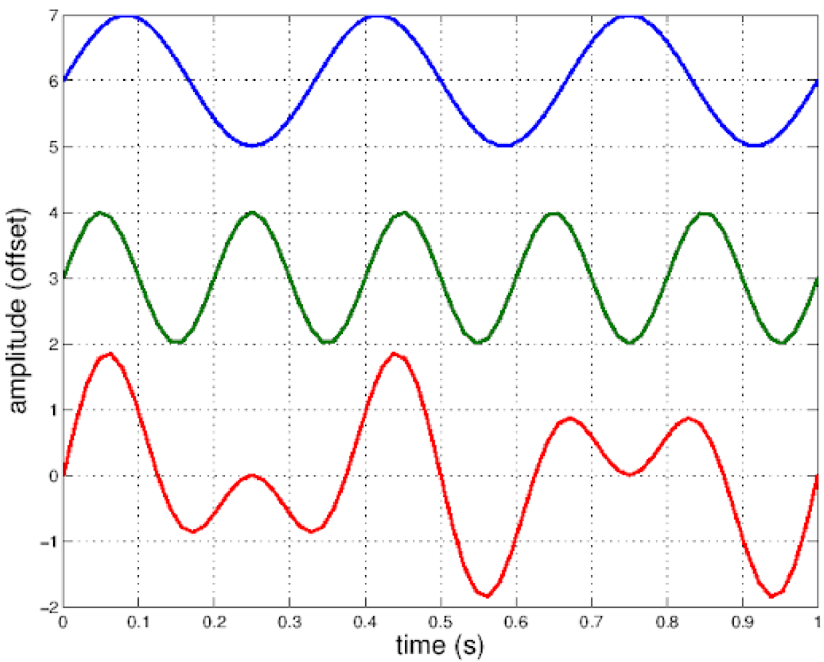
- .
- .
- .
- …add as many things as you can find

Interpret what you see

- .
- ...add as many things as you think are relevant

Observing – Describing: Warm-Up

Write down a bullet list of **observations** (= "what do you see?)



- Top two: continuous functions that periodically oscillate between two values
- Same constant amplitude (+/- 1 unit), but offset along y is different (+6 for blue, +3 for green)
- different frequencies/repeat distance (0.34; 0.2 respectively) that are not related by an integer
- Third: continuous, irregular function that appears similar to the top two but:
  - amplitude is **not** constant = fluctuates within an interval at offset of (approximately) -2 to +2
  - no detectable repeat distance

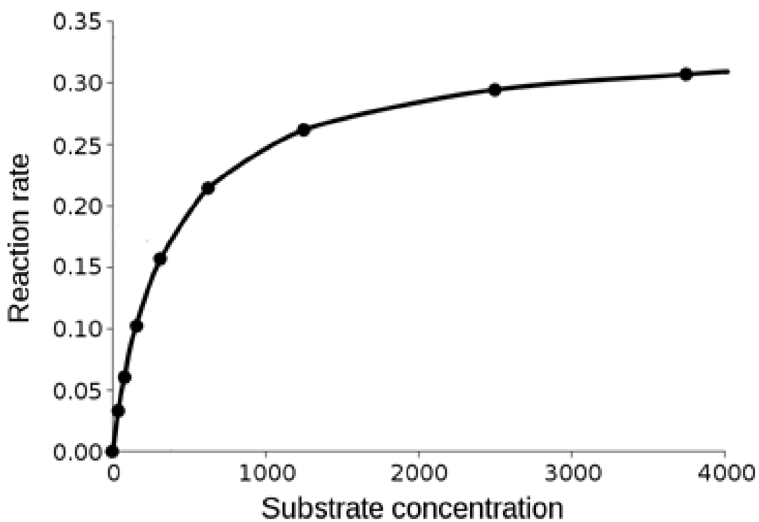
Interpret what you see

- Two sine functions
- Third function is the sum of the first two
  → it is irregular because the frequencies of component waves do not relate to each other through an integer

Observing – Describing #1

Write down a bullet list of **observations**

- .
- .
- .
- ..add as many as you can find

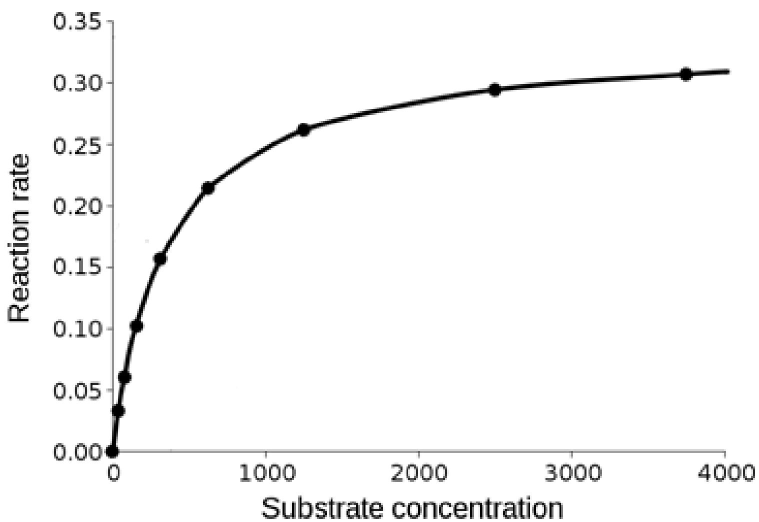


Interpretation

- .
- .
- .
- …add what you think is relevant

Observing – Describing #1

Write down a bullet list of **observations**



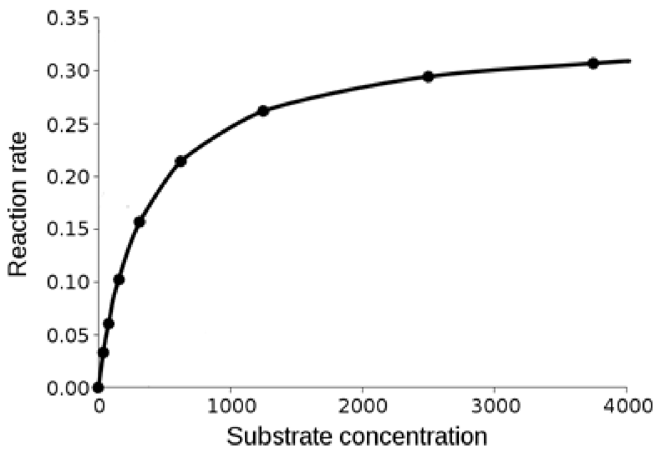
- Plot of a function, fitted to single data points
- Rate (y) vs substrate (x)
- Linear scales; arbitrary units
- Linear at start (x= 0)
- Asymptotic for large x
- **No error bars**
- **Perfect fit for the entire graph**

Interpretation

- Hyperbolic function
- Reaction will reach a maximum rate = saturation beyond which rate becomes independent of substrate concentration
- ➔ saturation implies that the reaction requires a physical interaction that at some point becomes rate limiting.
- This is not based on actual experimental data = just an illustration

- This is an example for enzyme kinetics

Takeaway



If the data is a plot of a function you want take note of

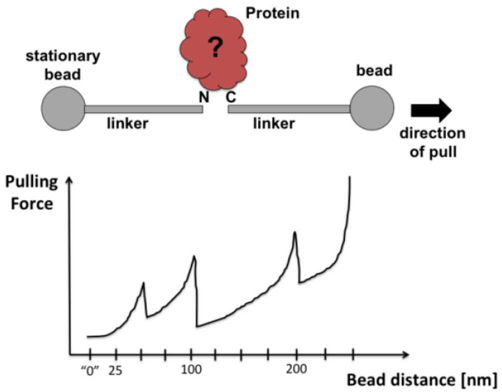
- Plot of what vs what & units (if given)?
- Axes?
  - linear? log?
- Shape of Function?
  - continuous vs discontinuous?
  - simple?
    - linear? exponential? periodic?
  - complex/irregular?
- Sampling?
  - continuous? discrete? → interval?
  - processed/fitted vs raw?

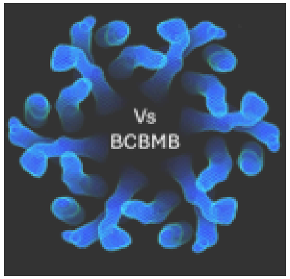
- Magnitude of Change?
- Location(s) and # of Significant Change(s)?
- Special Behaviors at Start/End?

At first, the number of points to consider may seem overwhelming and/or over the top. Yet – all of these aspects are important for representing or interpreting data….. let me demonstrate this to you….

TASK 3

The picture shows you the general idea of an approach to study questions related to protein folding. Specifically: a rigid linker molecule is used to attach the N-terminus (N) of the protein to a stationary bead (left), while a second rigid linker molecule attaches the C-terminus (C) to a bead whose position can be manipulated and monitored (right). One type of experiment that is carried out with such a setup is to pull on the movable bead while watching how its position changes with respect to the other bead as the force of the pull increases. A potential outcome of such an experiment – plotting pulling force vs distance of the two beads – is shown in the lower part of the figure.





- Plot of what vs what & units (if given))? Force (no units/intervals given) vs distance [nm]
- Axes?
  - Force (can't tell - assume linear)
  - distance linear
- Shape of Function?
  - continuous
  - complex/irregular
    - exponential – linear drop – exponential …. asymptotic
  (based on assumption)
- Sampling?
  - continuous
  - raw (no error bars)
- Magnitude of Change? Force - can't tell but baseline trends up, distance: 250nm total
- Location(s) and # of Significant Change(s)?
  - 3 distinctive events/drops at 50,100,200nm
- Special Behaviors at End? constant (start), asymptotic (end)

==> distance increases as more force is applied = polymer goes from a compact/organized state to a less organized state ➔ this shows an unfolding trajectory

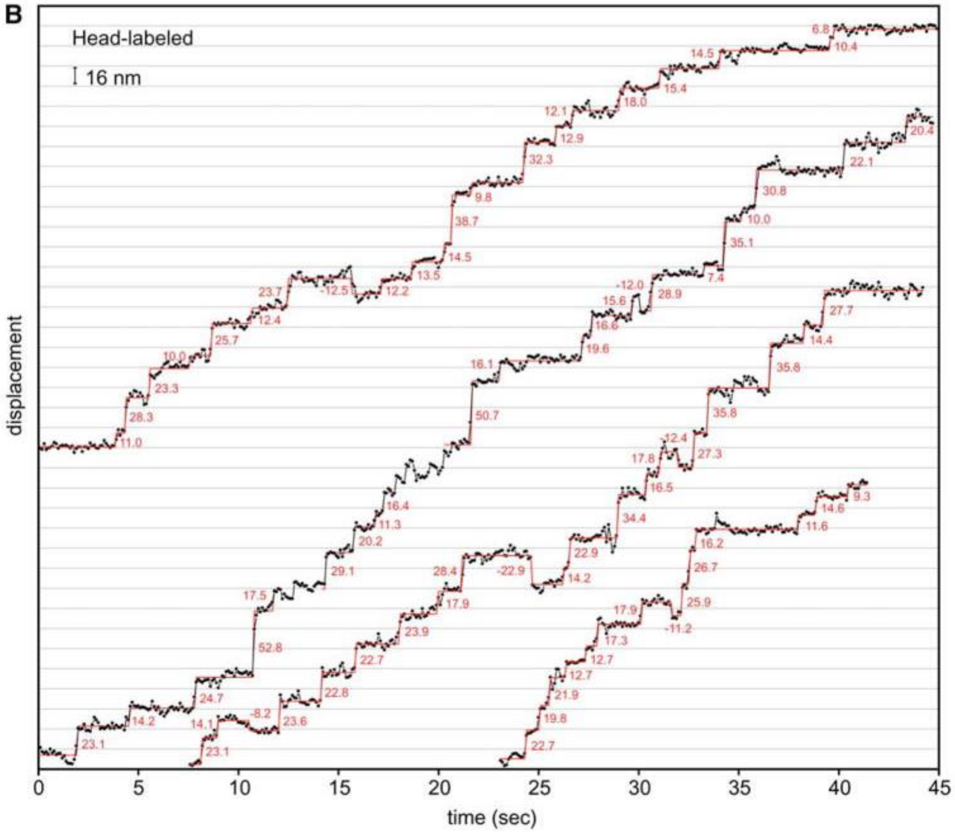
==> x-axis is linear = overall this is a gradual process

==> exponential leading to linear drops = two shapes = two different types of events; exponential regions reflect a smooth and incremental change; drops signify a sudden change involving multiple intramolecular interactions at once; asymptotic behavior indicates total length of polymer …once you know more about protein stats you can use this to calculate the # of amino acids in this protein

==> single molecule measurement of unfolding a single protein chain

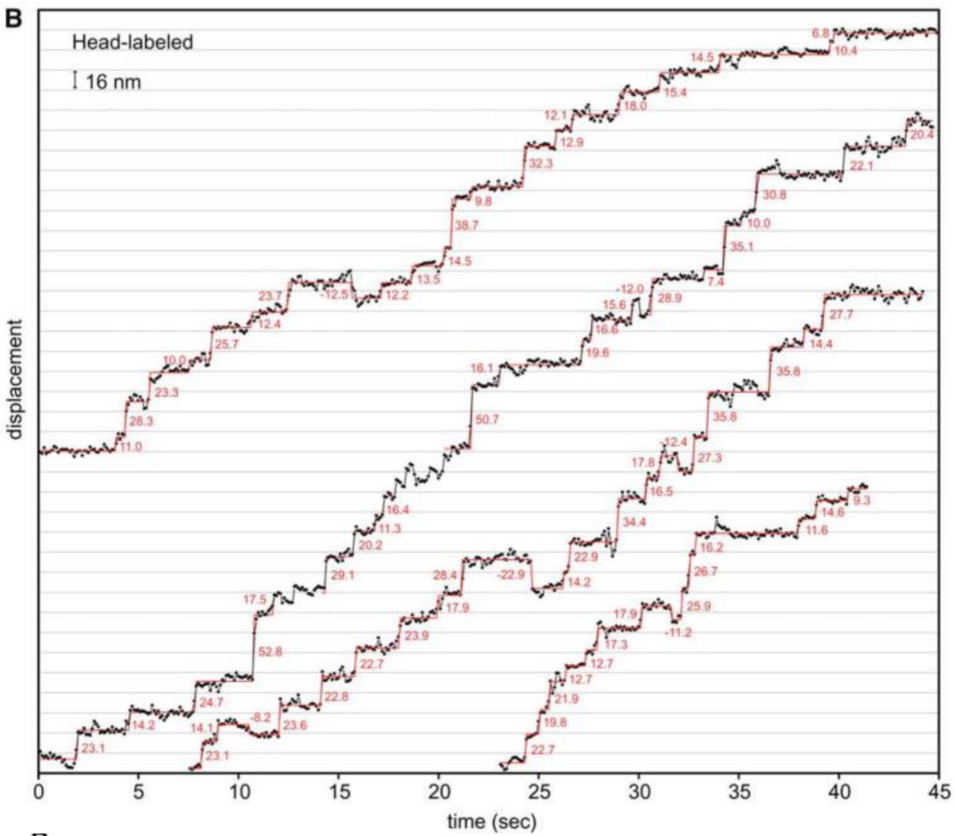
==> spacing between events tells you that each event corresponds to disruption of a separate protein domain (linear drops) and unraveling of the domains secondary structure elements (exponential regions)

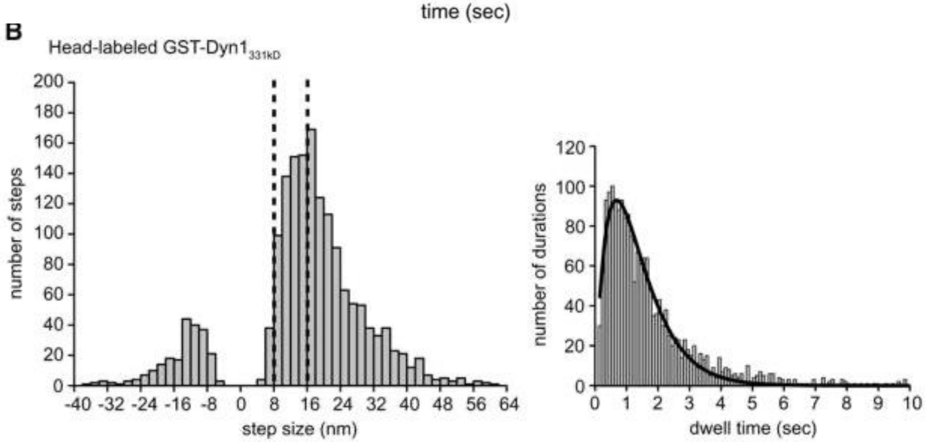
Observing – Describing #2



A much more advanced example….try!

Observing – Describing #2



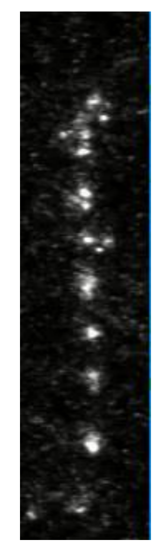


These plots are data from single molecule measurements.

Process studied: stepping of dynein motor proteins on microtubule tracks.

Observation: 4 molecules are tracked; linear axes; see mostly "pseudo" linear behavior; 16nm increment in y → data seem discrete; sometimes see molecule reverse course and moving backwards (negative values for y); duration (x) is not constant;

Dynein
speed x100

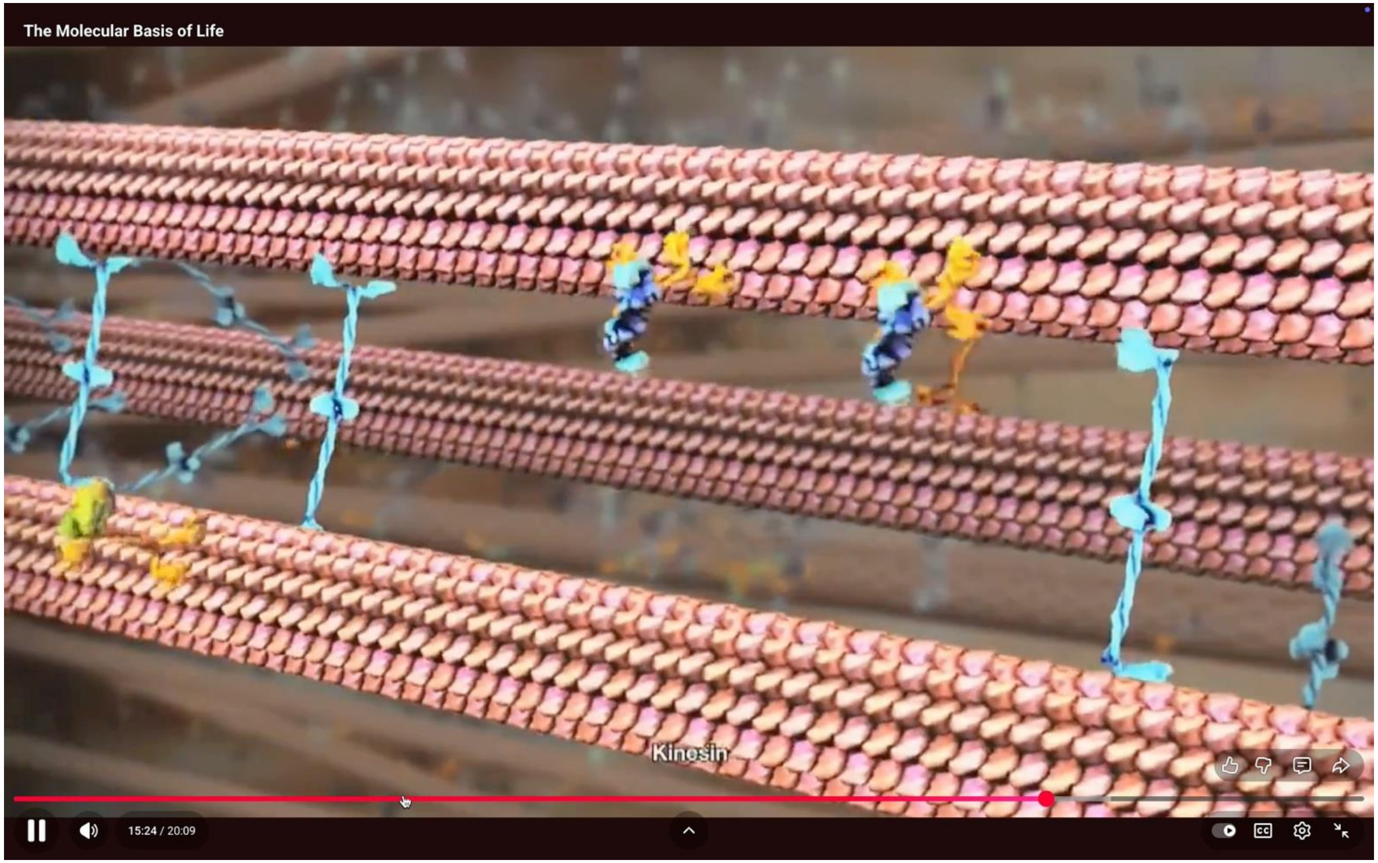


Reck-Peterson et al (2006) Cell 126:335-348

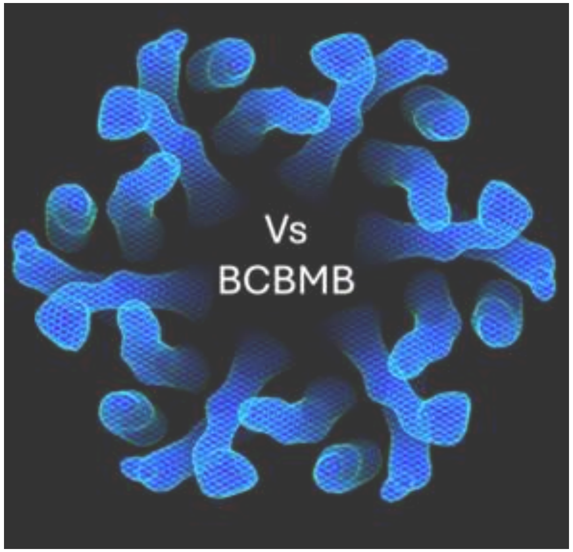
Microtubule – Motor Mechanism – Dynein Walk

Original Full Video: "The Molecular Basis of Life"

https://www.youtube.com/watch?v=fpHaxzroYxg



Based on the data you just looked at ….do you notice the inaccuracy in this animation? Does it matter?



Slides are freely available at
vsbcbmbstudy.com

If you found this primer on how to fix "data blindness" helpful and would like to review the content live (where you can ask questions), and/or get additional practice examples – use the QR code to visit my "workshops" page & to register for a 50min online workshop "Observation to Description"