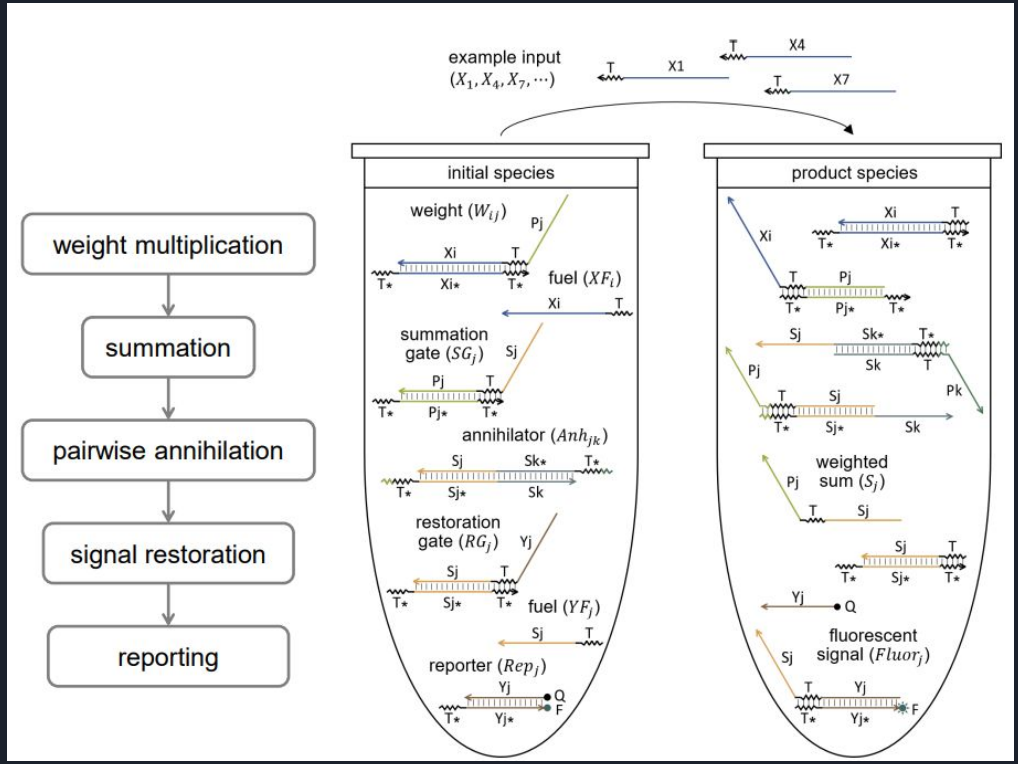
Deliverable DNA Circuits

Kyle McGraw

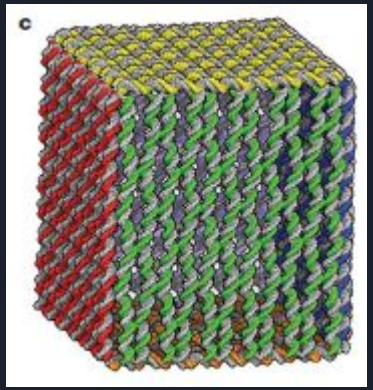
Limitations of Our DNA Circuits

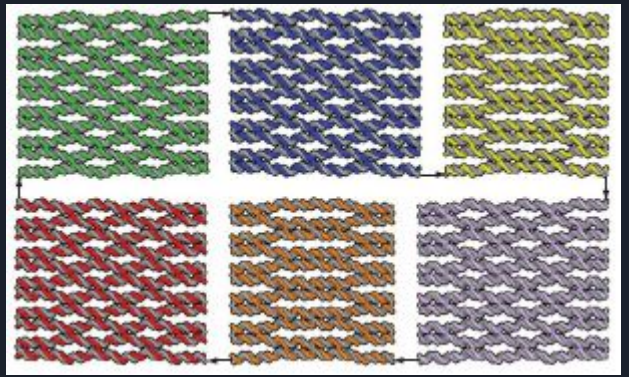
- Unlimited possibilities
- Complex functions in a test tube
- How can we deliver a circuit to a place in the body?
- Can we release the circuit upon interaction with some signal?



DNA Origami Box

- Container for DNA circuit
- Could be used for drug delivery
- Can we design a box to bring store then release a whole DNA circuit?
- Next step: create an openable lid

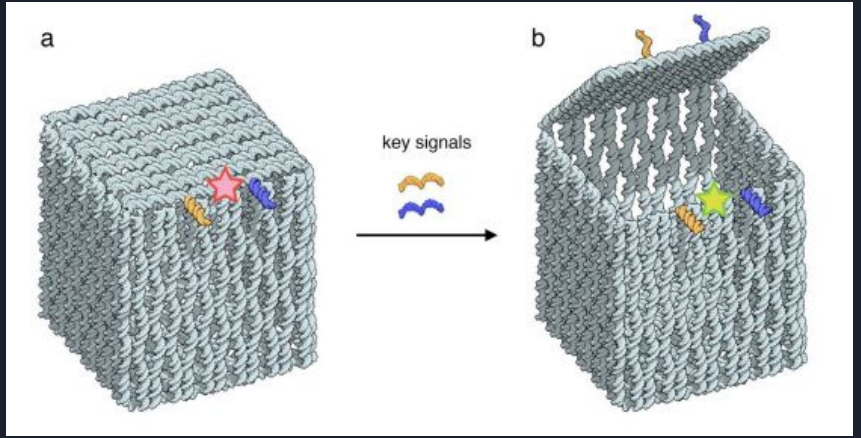




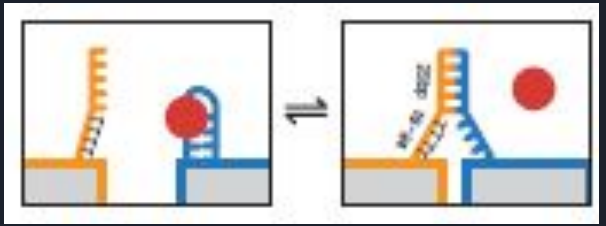
Andersen, E., Dong, M., Nielsen, M. *et al.* Self-assembly of a nanoscale DNA box with a controllable lid. *Nature* 459, 73–76 (2009). https://doi.org/10.1038/nature07971

Controllable Lid

- Key and lock system
  - Strand displacement
  - Aptamer or other such strand that can sense a target protein
- Additional elements needed
  - Enclosed circuit in box
  - Design a key to activate the circuit
  - Release key when box opened



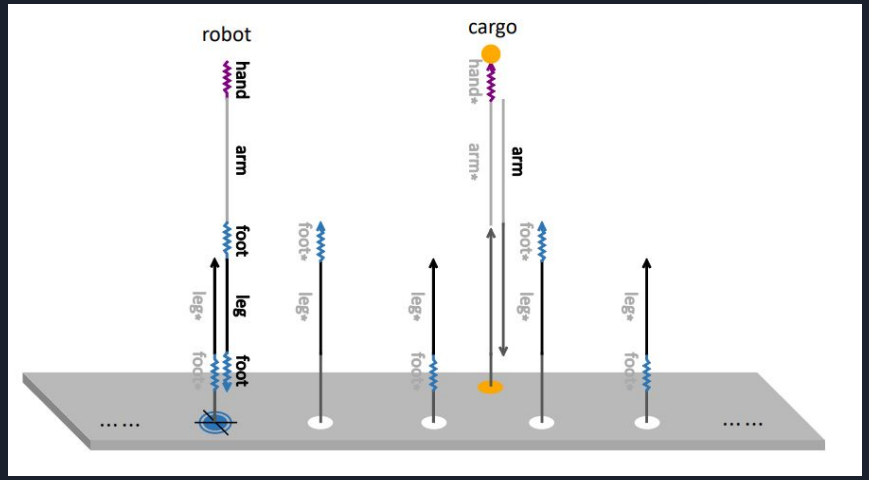
Andersen, E., Dong, M., Nielsen, M. *et al.* Self-assembly of a nanoscale DNA box with a controllable lid. *Nature* 459, 73–76 (2009). https://doi.org/10.1038/nature07971

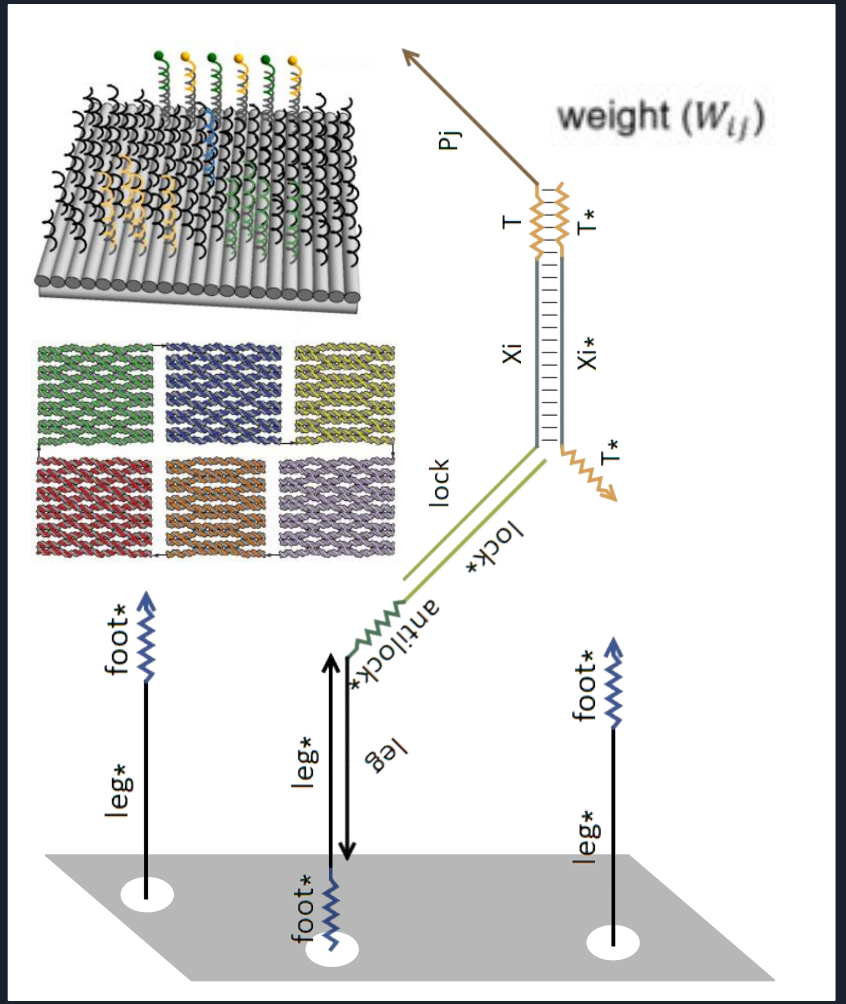


Douglas, S. M., Bachelet, I., & Church, G. M. (2012). A logic-gated nanorobot for targeted transport of molecular payloads. *Science*, 335(6070), 831–834. https://doi.org/10.1126/science.1214081

Tethered Circuits

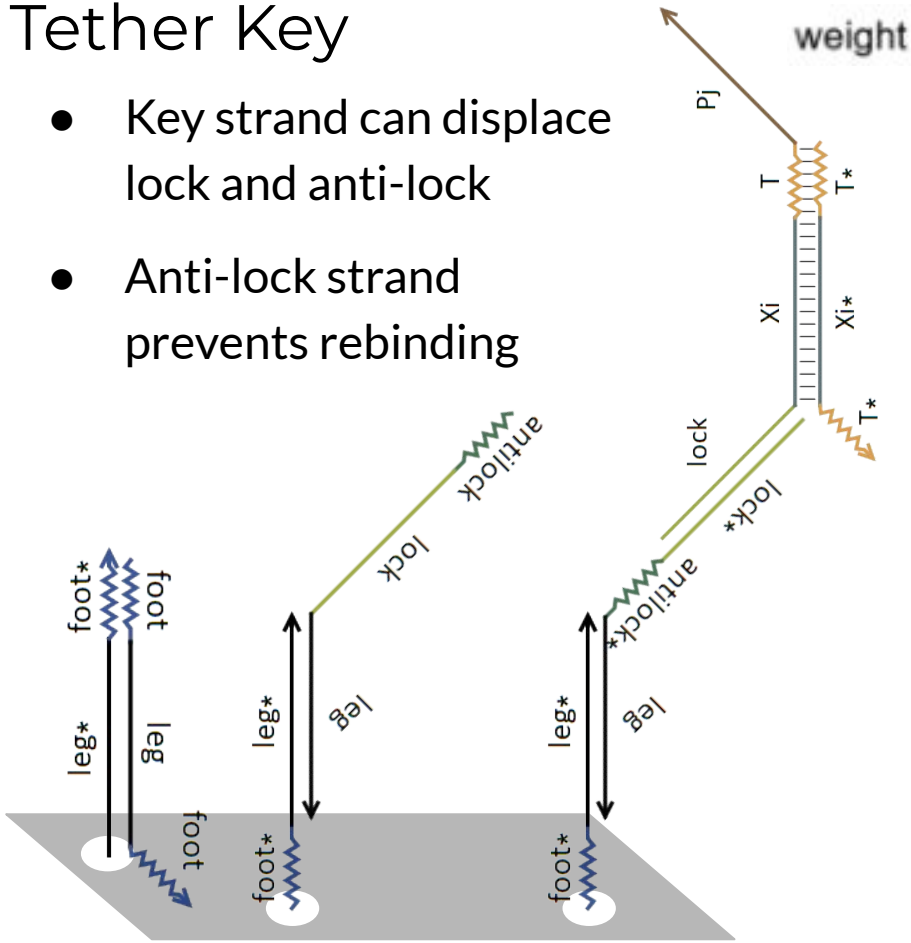
- Tether circuit to the inside of box
  - Similar to our cargo
- Lock strand will be useful for next step

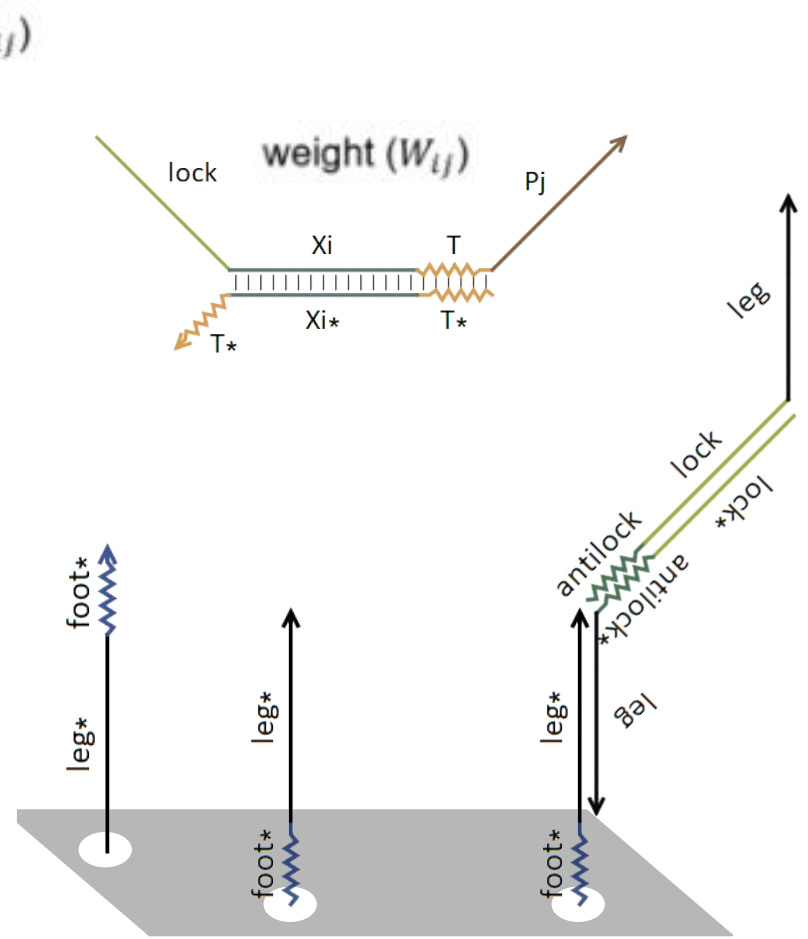




Tether Key

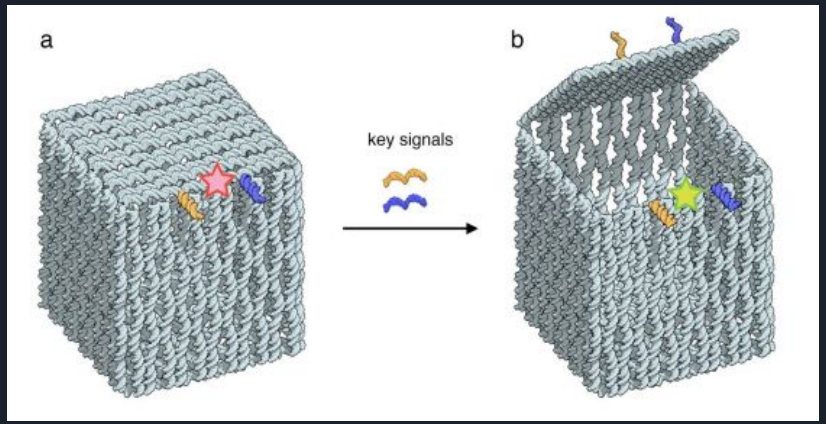
- Key strand can displace lock and anti-lock
- Anti-lock strand prevents rebinding

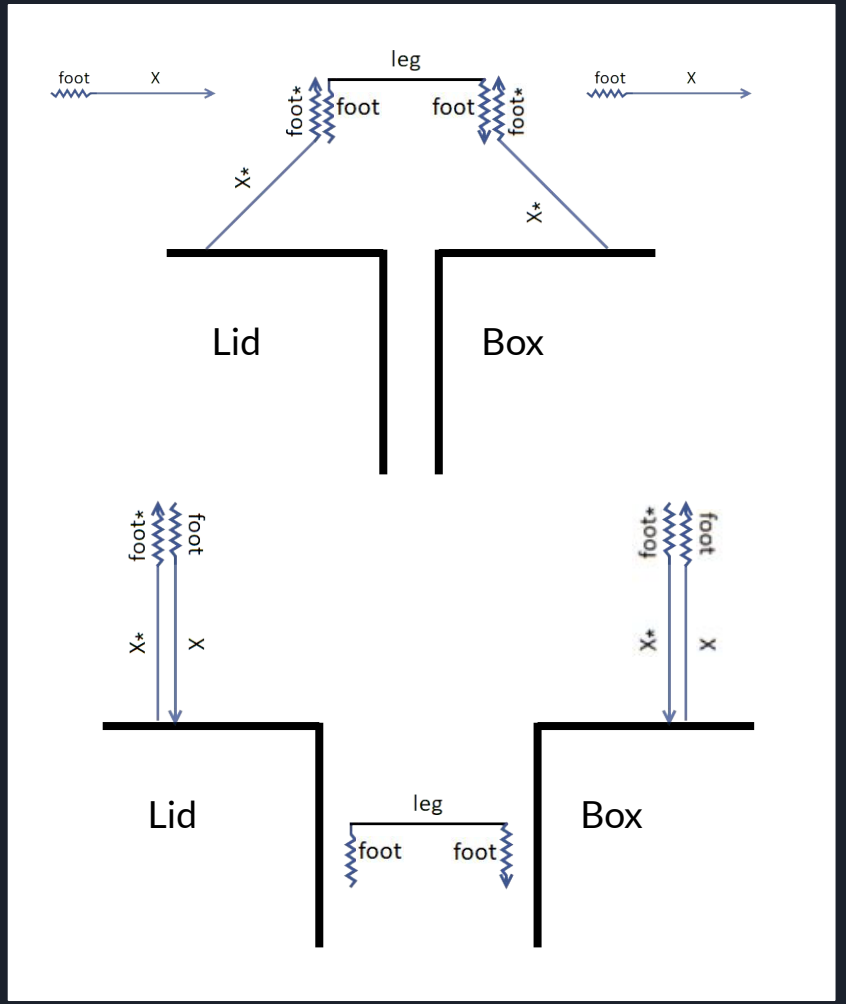




Key Release

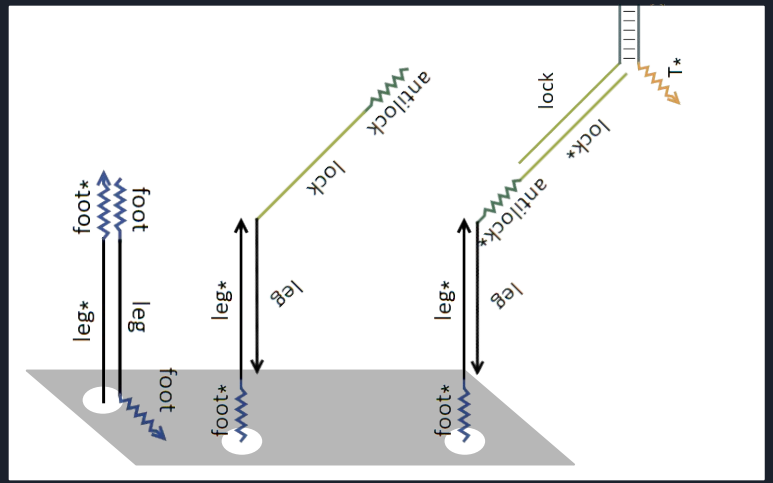
- Key clasps the lid closed
- Opening lid releases key

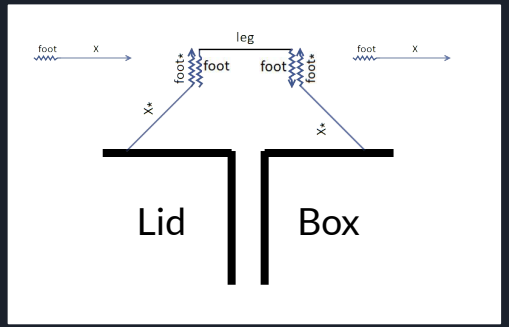


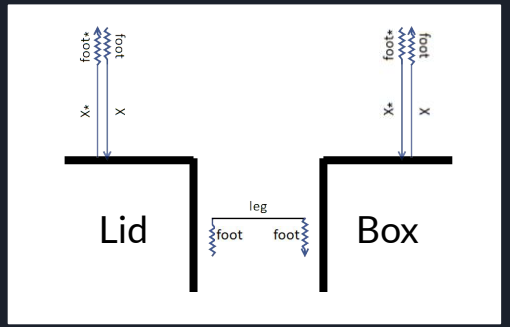


Limitations/Improvements

- The lock/anti-lock system could be improved
  - Both strands can bind to the track before each other
  - Design a hairpin structure so that it folds up
- Key system could be improved
  - Key has to bind to the track and key clasp may not be strong enough
  - Make key already tethered to the track but connected to an inhibitor
  - Opening box releases an activator strand could remove the inhibitor strand
  - Longer domains for the clasp bonds







References

Andersen, E., Dong, M., Nielsen, M. *et al.* Self-assembly of a nanoscale DNA box with a controllable lid. *Nature* 459, 73–76 (2009). https://doi.org/10.1038/nature07971

Douglas, S. M., Bachelet, I., & Church, G. M. (2012). A logic-gated nanorobot for targeted transport of molecular payloads. *Science*, 335(6070), 831–834. https://doi.org/10.1126/science.1214081

Amir, Y., Ben-Ishay, E., Levner, D. *et al.* Universal computing by DNA origami robots in a living animal. *Nature Nanotech* 9, 353–357 (2014). https://doi.org/10.1038/nnano.2014.58