

# Life Detection and Viruses as Biosignatures

Kathryn Bywaters

# Astrobiology

**“The search for life's origin, evolution, distribution, and future in the universe”**

- To understand distribution we need to be able to detect life – but what is life?
- In the absence of a theory of life, it is defined by its properties.
- Life is a self-enclosed, self-sustained chemical system capable of undergoing Darwinian evolution.

# NASA's Life Detection Ladder

- Rung (evidence of life)
  - Darwinian Evolution
  - Growth and Reproduction
  - Metabolism
  - Molecules & Structures Conferring Function
  - Potential Biomolecule Components
  - Potential Metabolic Byproducts
  - Biofabrics

# NASA's Life Detection Ladder

- Molecules & Structures Conferring Function
  - Polymers that support information storage and transfer for terran life (DNA, RNA)
- NASA Astrobiology Strategy 2015 “Weird Life”
  - “An alien biochemistry might not have the same chemistry exhibited in Earth-based life”
- Universal feature of life
  - On Earth - molecules encoding genetic data necessary for the functioning and replication of life will be organized in the form of polyanionic or polycationic polymers (Benner and Hutter 2002)

# Instrument Development

Looking for *in situ* biosignatures

- Intact detection
  - High-resolution microscopy devices
  - Detection of proteins in capsids
  - Nanopore-based electrical sensing
- Molecules conferring function
  - Benner's Instrument
  - Nanopore- based electrical sensing



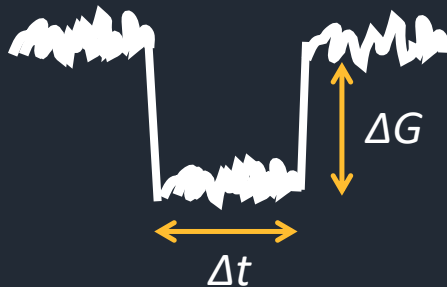
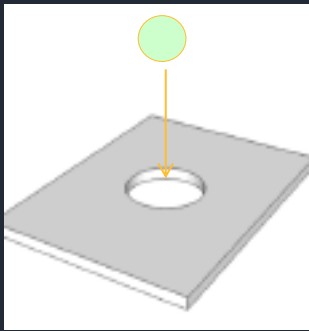
# Instrument Development

## NASA's Concept and Instrument Development Proposals

- NIAC: TRL 1-2
- PICASSO: TRL 1-3
- MatISSE: TRL 4 and over



# Nanopore Technology – Overview



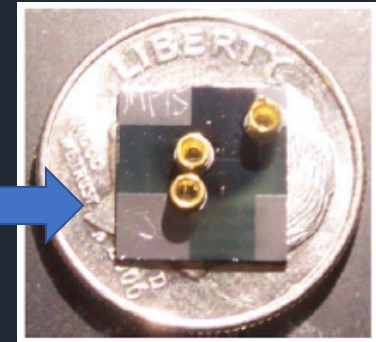
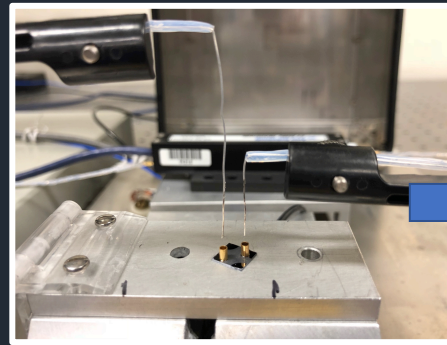
Blockade event shape with depth ( $\Delta G$ ) and duration ( $\Delta t$ )

- Nanopore spans a membrane between two compartments containing an electrolyte solution
- Voltage is applied & an ionic current established through the nanopore
- As a particle translocates the nanopore is blocked for a short period, during which a current drop can be recorded

# Nanopore Technology for Life Detection

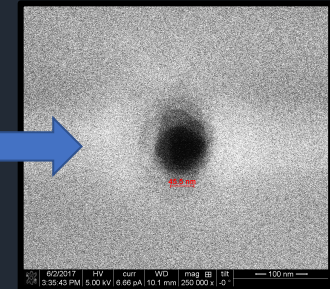
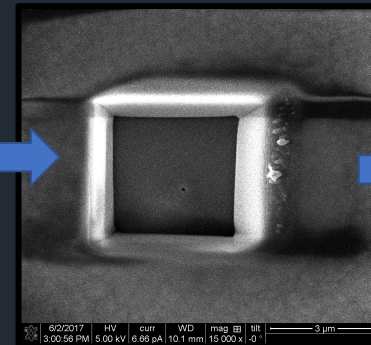
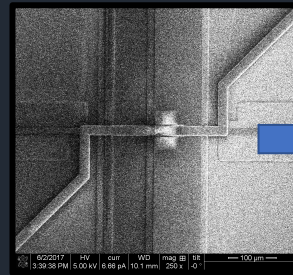
## Biological nanopore technology

- Commercially available
- Operated on the ISS
- Limitations:
  - Stability
  - Specificity (DNA and RNA only)



## Solid-state nanopore technology

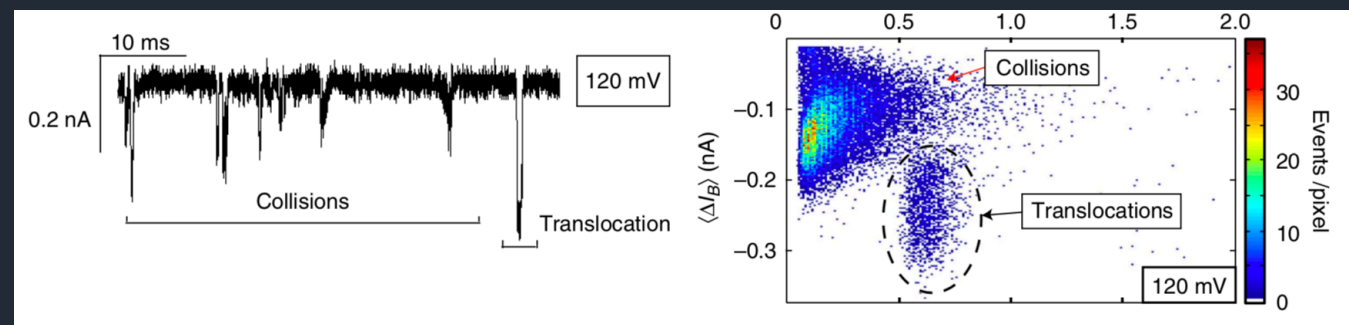
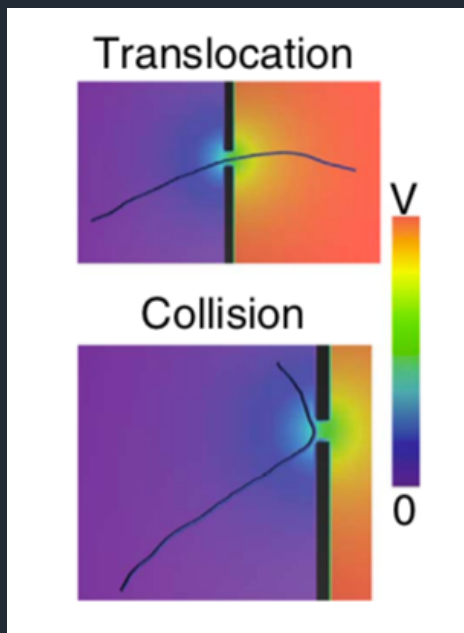
- Versatile
  - Different pore diameters for the detection of multiple types of biomarkers
- Robust





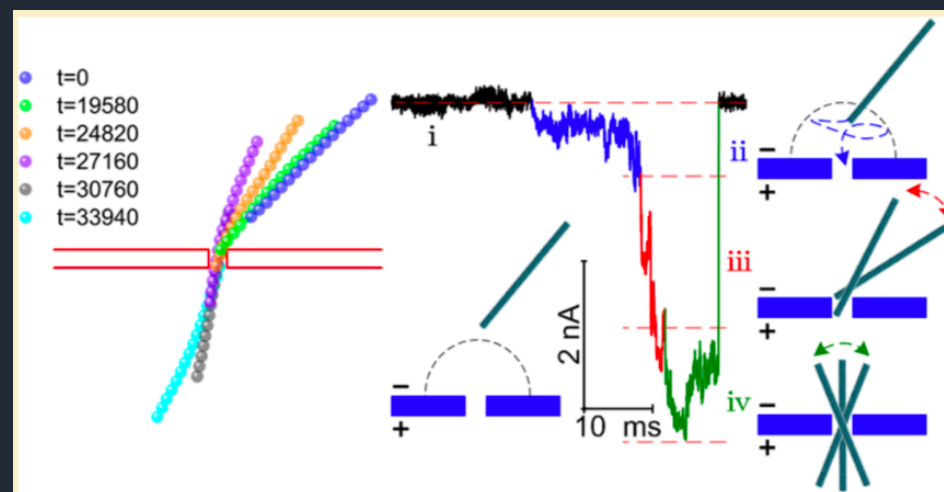
McMullen, Angus, et al. "Stiff filamentous virus translocations through solid-state nanopores." *Nature communications* 5 (2014): 4171.

- Stiff filamentous virus fd
- Electric field distribution aligns an approaching fd with the nanopore
- fd is too stiff to translocate in folded configurations, therefore translocates linearly

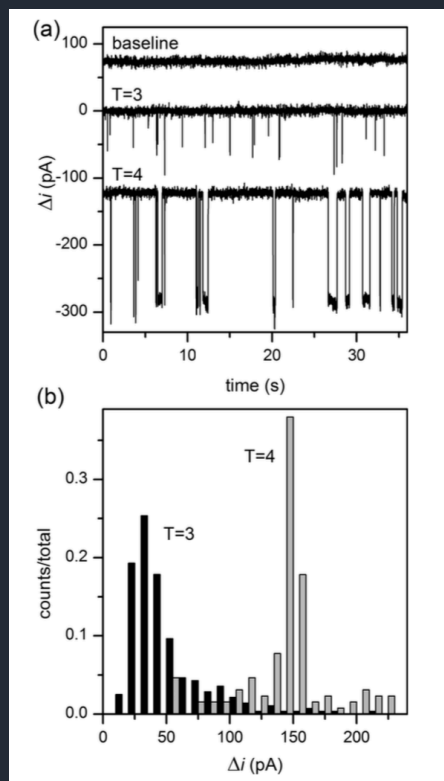


Wu, Hongwen, et al. "Translocation of rigid rod-shaped virus through various solid-state nanopores." *Analytical chemistry* 88.4 (2016): 2502-2510.

- Translocation of rigid rod-shaped tobacco mosaic virus
- Due to the high rigidity three types of events with distinctive characteristics at the capture process and a strong current fluctuation during the translocation of TMV



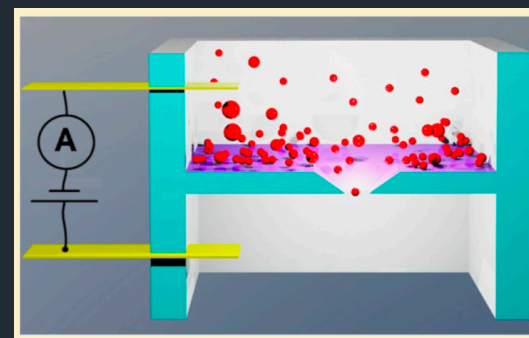
Zhou, Kaimeng, et al. "Characterization of hepatitis B virus capsids by resistive-pulse sensing." *Journal of the American Chemical Society* 133.6 (2011): 1618-1621.



- HBV capsids assembled in vitro from Cp149
- Assembled T = 3 (90 Cp149 dimer) and T = 4 (120 dimer) capsids are 31 and 36 nm in diameter
- Easily discriminated by monitoring the change in current as capsids passed through an electrically biased pore.

Arjmandi, Nima, Willem Van Roy, and Liesbet Lagae.  
 "Measuring mass of nanoparticles and viruses in liquids with nanometer-scale pores." *Analytical chemistry* 86.10 (2014): 4637-4641.

- Measured mass of nanoparticles and viruses and their sedimentation (provided estimate for the nanoparticle mass-density)
- Low concentration and small volumes



	measured by solid-state nanopore		
	radius of capture zone ( $\mu\text{m}$ )	size (nm) <sup>b</sup>	density ( $\text{g}/\text{cm}^3$ ) <sup>b</sup>
polystyrene nanoparticle	21	$355 \pm 14$	$1.6 \pm 0.3$
gold-citrate nanoparticle	22.5	$110 \pm 8$	$19 \pm 1.1$
HIV virions	8.25	$190 \pm 14$	$1.2 \pm 0.1$
EBV virions	7.8	$160 \pm 11$	$1.9 \pm 0.2$
polystyrene nanoparticle	9.5	$217 \pm 10$	$2 \pm 0.4$

Janjic, Aleksandar. "The Need for Including Virus Detection Methods in Future Mars Missions." *Astrobiology* 18.12 (2018): 1611-1614.

- We don't really know how and when viral units were created on Earth.
- The virus-first hypothesis is controversial and difficult to falsify, which makes it a very weak hypothesis (only falsifiable hypotheses are suitable for knowledge gain).
- The exploration of Mars can finally close this knowledge gap, if viral units actually arise before cells.
- If we only find viral units on Mars, but no cells, this can only be explained by the virus-first hypothesis (since cells, if they existed, would be better conserved).
- If viral entities did exist on Mars, this is the only way in the near future to falsify the virus-first hypothesis, which is not possible on Earth so far.
- If cellular units are found, the question of the formation of viruses only shifts and is still unclear.

Build It and They Will Come!