

# KAIST Grand Challenge 30 project

## 미토콘드리아 온도와 열생물학

### Mitochondrion temperature and thermal biology

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SHORT SHARP SCIENCE 4 May 2017

The energy generators inside our cells reach a sizzling 50°C



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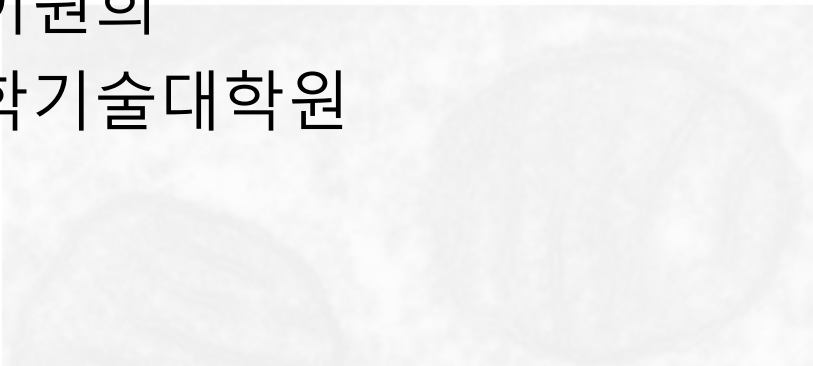
2017. 09.

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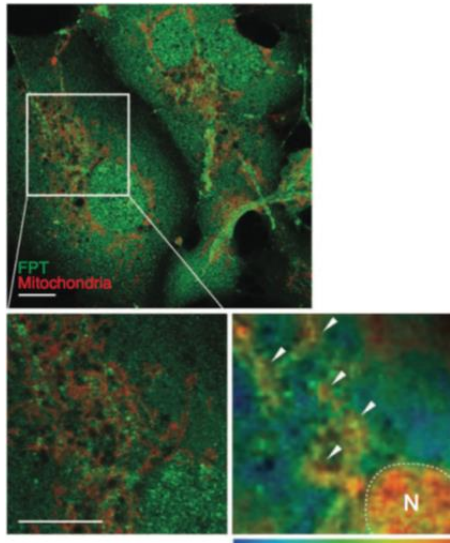
나노과학기술대학원

Mitochondria found to run as high as 50 C

May 10 2017 by Bob Virda report



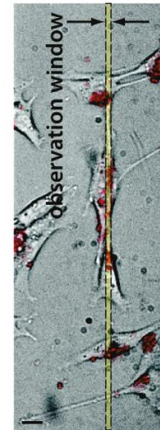
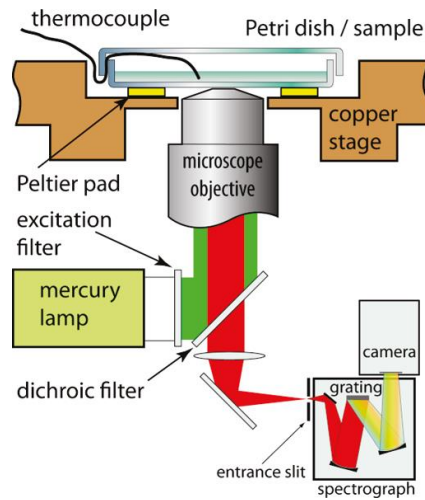
# Intracellular thermometry



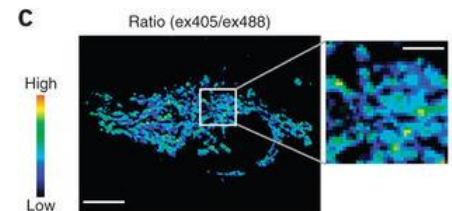
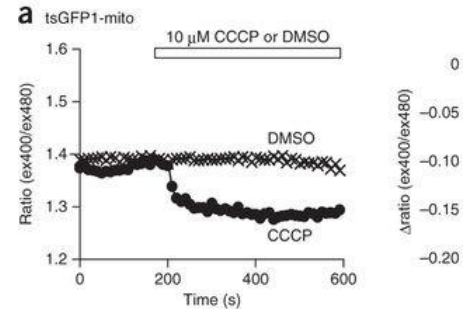
5.4 (31 °C)

6.5 (35 °C)

Okabe et al. *Nat Comm* 2012



Yang et al. *ACS Nano* 2011



Kiyonaka et al. *Nat Method* 2014

Nano thermometers: Fluorescence (Europium (III) thenoyltrifluoroacetate trihydrate, Au nanoclusters, synthetic polymers, GFP), nanodiamonds spin, QD,

**Local cell temperatures** investigated with “nano thermometers”  
→ Several results show **temperature changes > 1K**

What is the meaning of local temperature at nanoscale?

**Highly complex nanostructure**

**Material inhomogeneity**

**Mass transport**

**Non-equilibrium, active biochemical reactions**

# Debates

$\Delta T \sim$  a few  $K$  does not make sense



Heat diffusion equation

$$c\partial_t T(\mathbf{r}, t) - \kappa \nabla^2 T(\mathbf{r}, t) = p(\mathbf{r}, t)$$

$$\rightarrow \Delta T = \frac{P}{\kappa L} = \frac{\text{Heat power}}{\text{thermal conductivity} \cdot \text{size of heat source}}$$

$p \sim 100$  pW,  $L = 10$   $\mu\text{m}$ ,  $\kappa \sim 1$  W /m·K

$$\Delta T \sim 10^{-5} \text{ K}$$

Even with consideration of smaller  $L$ , short burst of energy, membrane surface thermal resistance, required power is  $\sim 1$   $\mu\text{W}$ .  $10^5$  discrepancy cannot be explained!

(Baffou et al. Nat. Methods 2014)

## Rebuttal

- $\kappa \sim 0.6$  (W /m·K) for water and 0.1-0.2 for proteins
- Size of heat source in mitochondria  $< 100$  nm
- If Heat dissipation in short time (1s), required energy will be  $\sim 10$  nJ
- + Heterogeneity in the conductivity of intracellular component
- + Complexity in the nanostructures (membranes mostly) of organelles
- + Heat capacity can change with complex and highly organized structure



# Abnormally high T of mitochondria

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### Mitochondria found to run as high as 50 C

May 10, 2017 by Bob Yirka report



Turns Out The Powerhouse of Our Cells Could Be Running at a Scorching 50°C

CSH Cold Spring Harbor Laboratory

## bioRxiv beta

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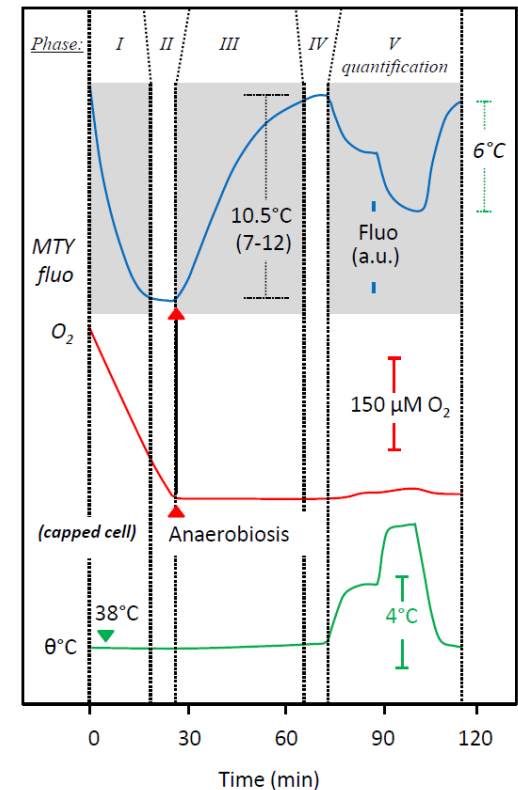
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### Mitochondria Are Physiologically Maintained At Close To 50 C

Dominique Chretien, Paule Benit, Hyung-Ho Ha, Susanne Keipert, Riyad El-Khoury, Young-Tae Chang, Martin Jastroch, Howard Jacobs, Pierre Rustin, Malgorzata Rak

doi: <https://doi.org/10.1101/133223>

- Metabolism at 50 °C?
- Protein stable at 50 °C?
- Is it true? Maybe mistake?
- Can we make use of it?



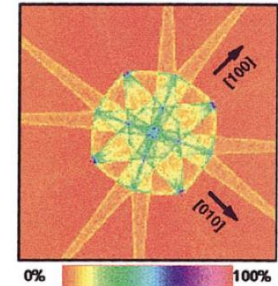
# Nanoscale temperature

- Kapitza thermal resistance
- Coherent Phonon experiments

- **What is TEMPERATURE?**

“Average energy of a system of particles”  $\langle K.E.i \rangle = \frac{m}{2N} \sum_n^N v^2(t_n) = \left\langle \frac{1}{2} m v_i^2 \right\rangle$

$$\left\langle \frac{1}{2} m v_i^2 \right\rangle = \frac{3}{2} k_B T_i \quad \text{or} \quad \left\langle \frac{1}{2} m v_i^2 \right\rangle = \frac{1}{4N} \sum_{\lambda, q} \hbar \omega_{\lambda}(q) \xi^{(i)2}(\lambda, q) \times \left( \frac{2}{e^{\hbar \omega_{\lambda}(q)/k_B T_i} - 1} + 1 \right)$$



Msal et al. PRL 2000

## Temperature defined locally vs. Length scale < phonon wavelength

- Nanoscale structure and materials
  - Thin films & superlattices
  - Nanotubes & nanowires
  - Graphene & 2D materials
  - Nanoparticles & QD



# Questions and Goals

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## Big question: **What is Temperature at nanoscale?**

1. Is the  $>1\text{K}$  temperature change by mitochondria possible?
  - Confirmation of the results
  - If not, what was wrong ?
  - If so, how is that possible ?
2. How to formulate effective  $T$  of molecules, or organelles?
  - Provide a *useful method* to describe  $T$  at nanoscale
3. Can we control nanoscale  $T$  in unusual manners?
  - Construct nanostructure with unusual heat transfer characteristics, such as super insulator.

# Methods

- Scanning thermal microscope

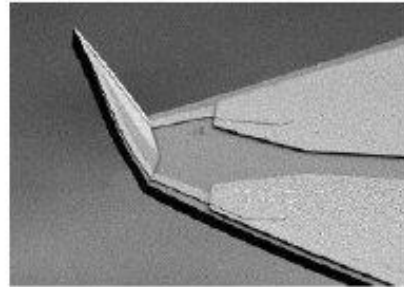
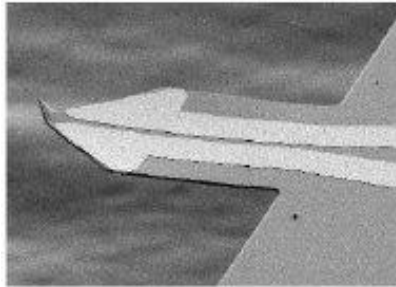
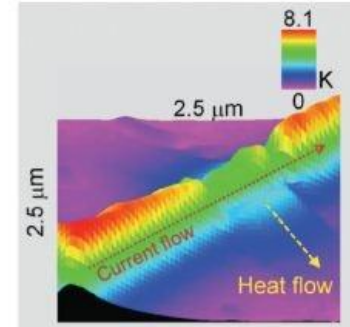
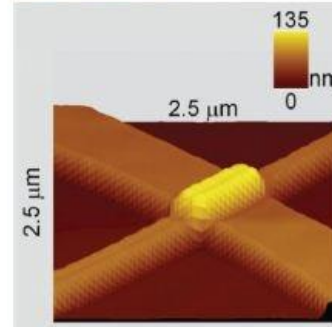
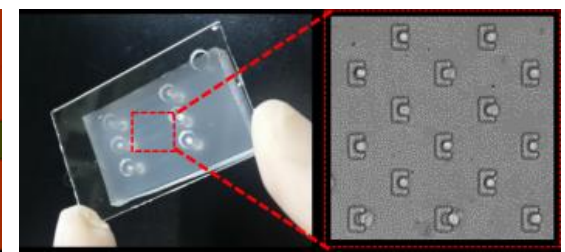
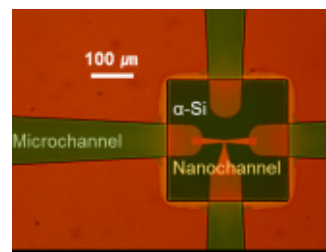
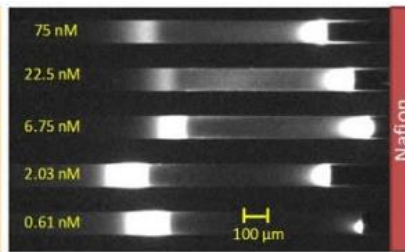
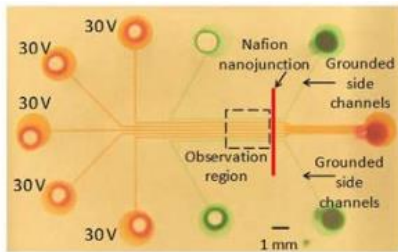


Figure 2(b and c)



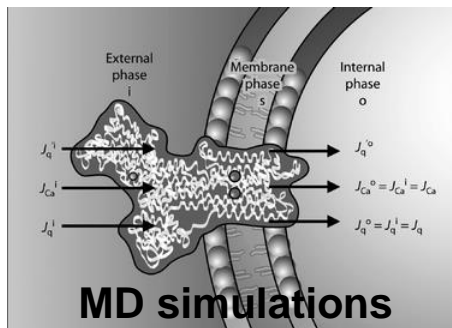
Courtesy of www.azonano.com

- Micro-, nanofluidics & nanofabrication (artificial cell, organelle)

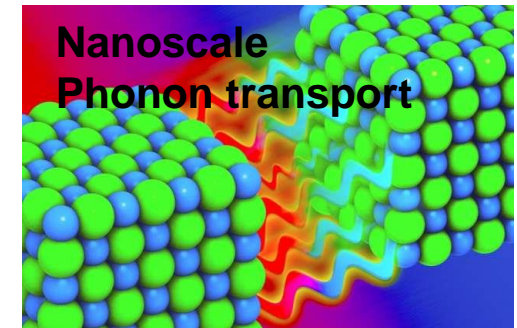
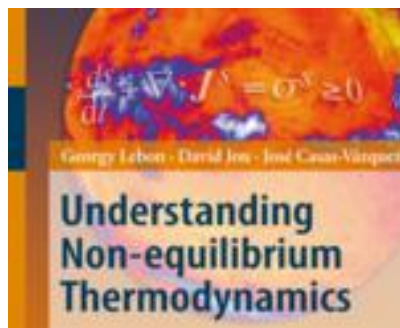


Chen et al. JACS 2011

- Active Collaborations



Bedeaux et al. PCCP 2008



# Why Grand challenge?

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- Temperature is one kind of basic physical parameter regulating life, yet poorly understood !!
- Difficulty in defining Nanoscale Temperature
- Importance of understanding nanoscale heat-transport : Nanodevice, nanomaterials, biology!
- Huge impacts on various fields, including nanoscale electronics, high-ZT, insulating material, cancer treatment etc.
- Not likely to be funded
- Not active, current research project of the lab