### **Designing patterns by controlling bacterial energetics**

#### Teuta Pilizota

Roger Land Building, teuta.pilizota@ed.ac.uk

## ATP and PMF are main free energy sources in *Escherichia coli*

A coarse-grain view of free energy coordination in *E.coli* 





# ATP and PMF are main free energy sources in Escherichia coli

ATP is loved by life because

 $ATP \rightarrow ADP + P_i$ 

gives 30-70 kJ/mol

Proton Motive Force (PMF) is an electrochemical gradient of protons:

$$PMF = \frac{kT}{e}\Delta pH + V_m$$

- powers  $F_1F_0$  ATPase
- drives the transport of sugars, amino acids and other substrates across biological membranes
- powers bacterial flagella motor





## PMF can be controlled via light activated proton pumps



Jessica M. Walter et al. PNAS 2007;104:7:2408-2412

### PMF can be controlled via light activated proton pumps



Videos in supplementary information here https://www.nature.com/articles/s41467-018-03161-8









### **PMF and ATP in disease**

Defects in oxidative phosphorylation have been implicated in neurodegenerative diseases such as Parkinson's (Parker, Parks, & Swerdlow, 2008) and Alzheimer's (Mutisya, Bowling, & Beal, 1994); while somatic mitochondrial DNA (mtDNA) mutational hotspots within ETC genes have been found in many types of cancer (Tan, Bai, & Wong, 2002) (Liu et al., 2001) (Polyak et al., 1998) (Jones et al., 2001). Indeed, Warburg hypothesized that the metabolic switch in which cancer cells choose to utilize aerobic glycolysis as their primary source of ATP, even in the presence of sufficient oxygen supply, was due to mitochondrial defects. However, it is now suspected that the mitochondria are reprogrammed to meet the high metabolic demands of cancer cells (Ward & Thompson, 2012). This highlights the necessity to engineer ways to shift the metabolic activity within a mammalian cell.

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