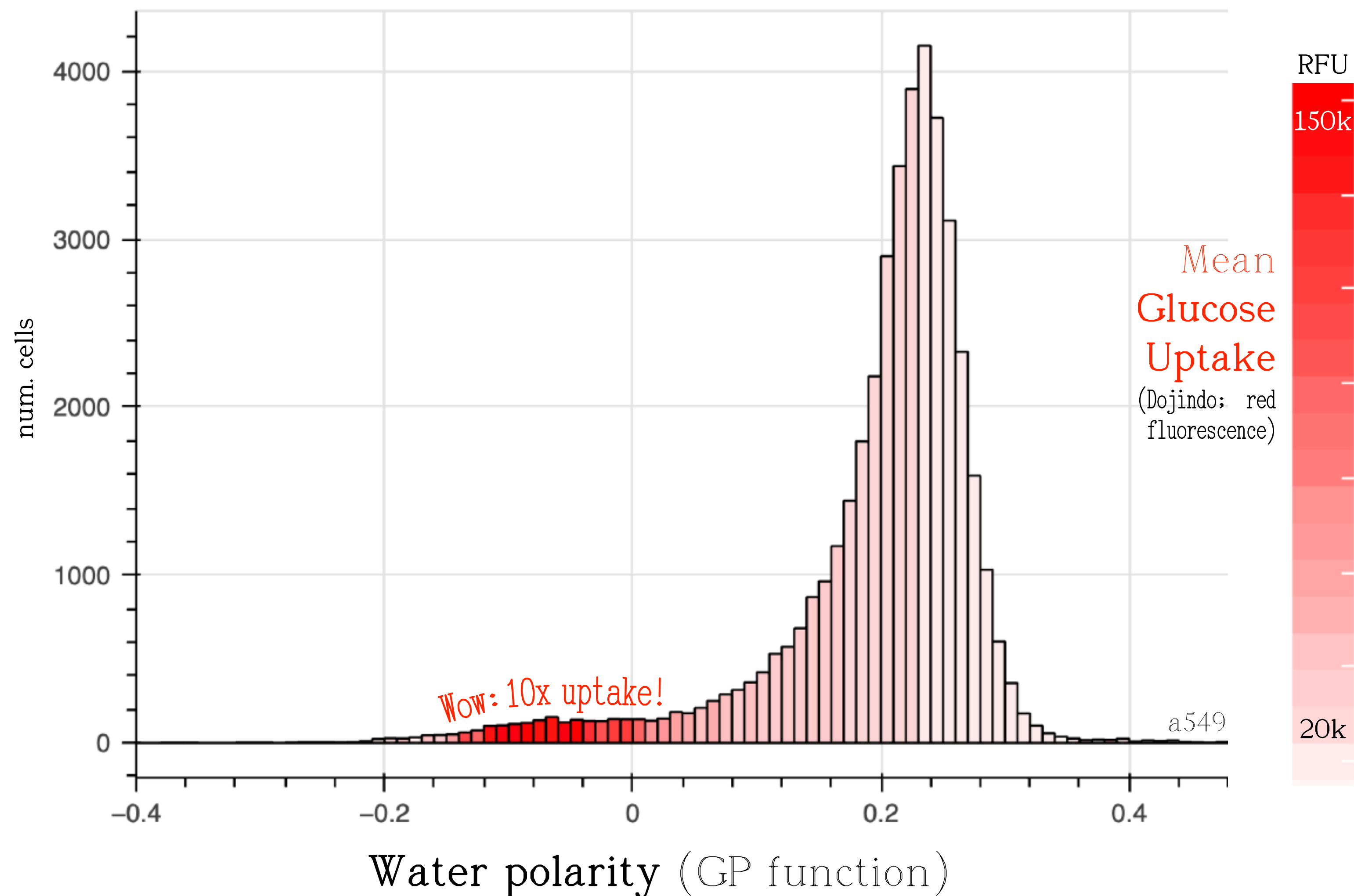
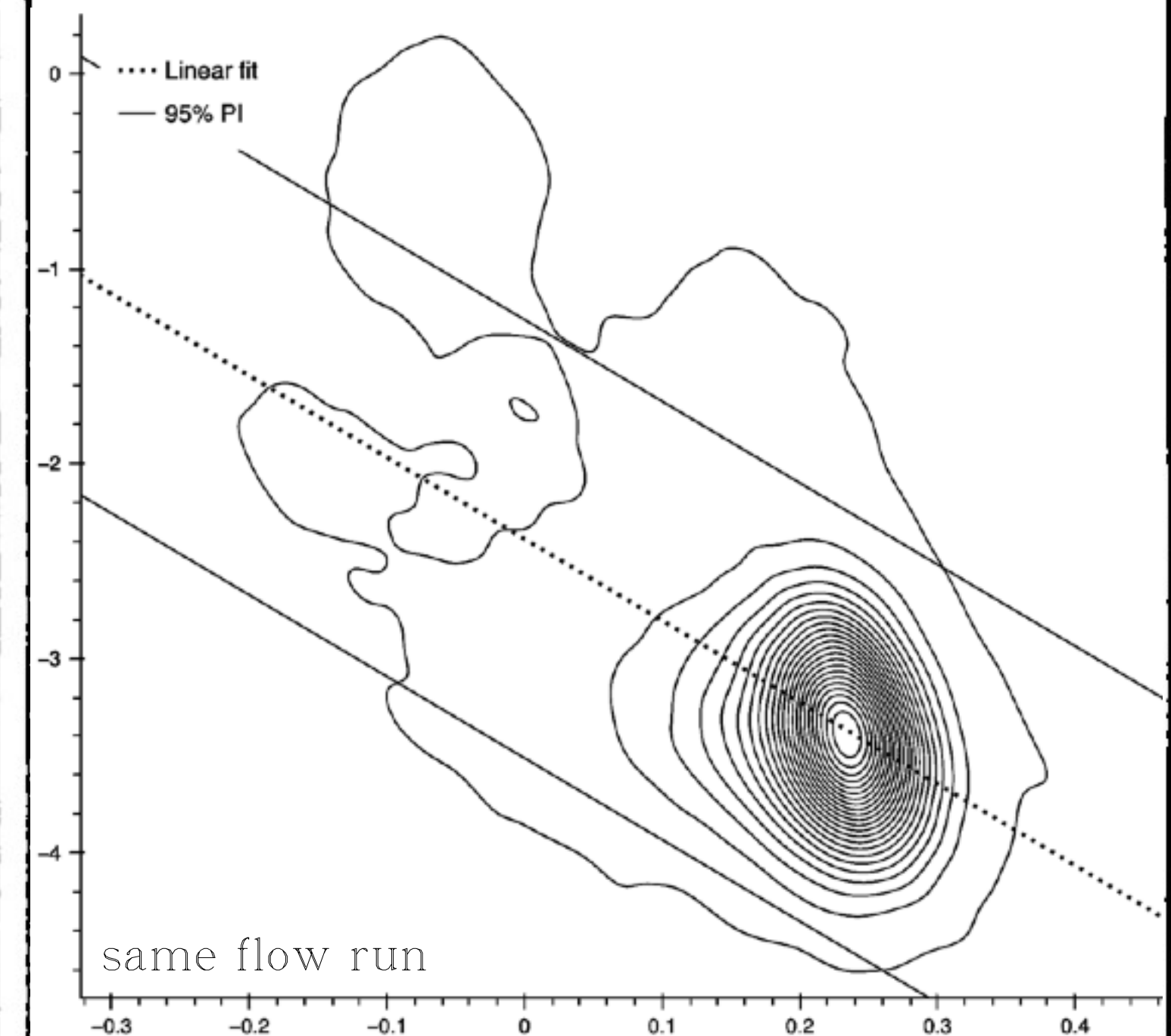


Glucose uptake is multiplied in depolarized water cancer cells: Warburg effect?



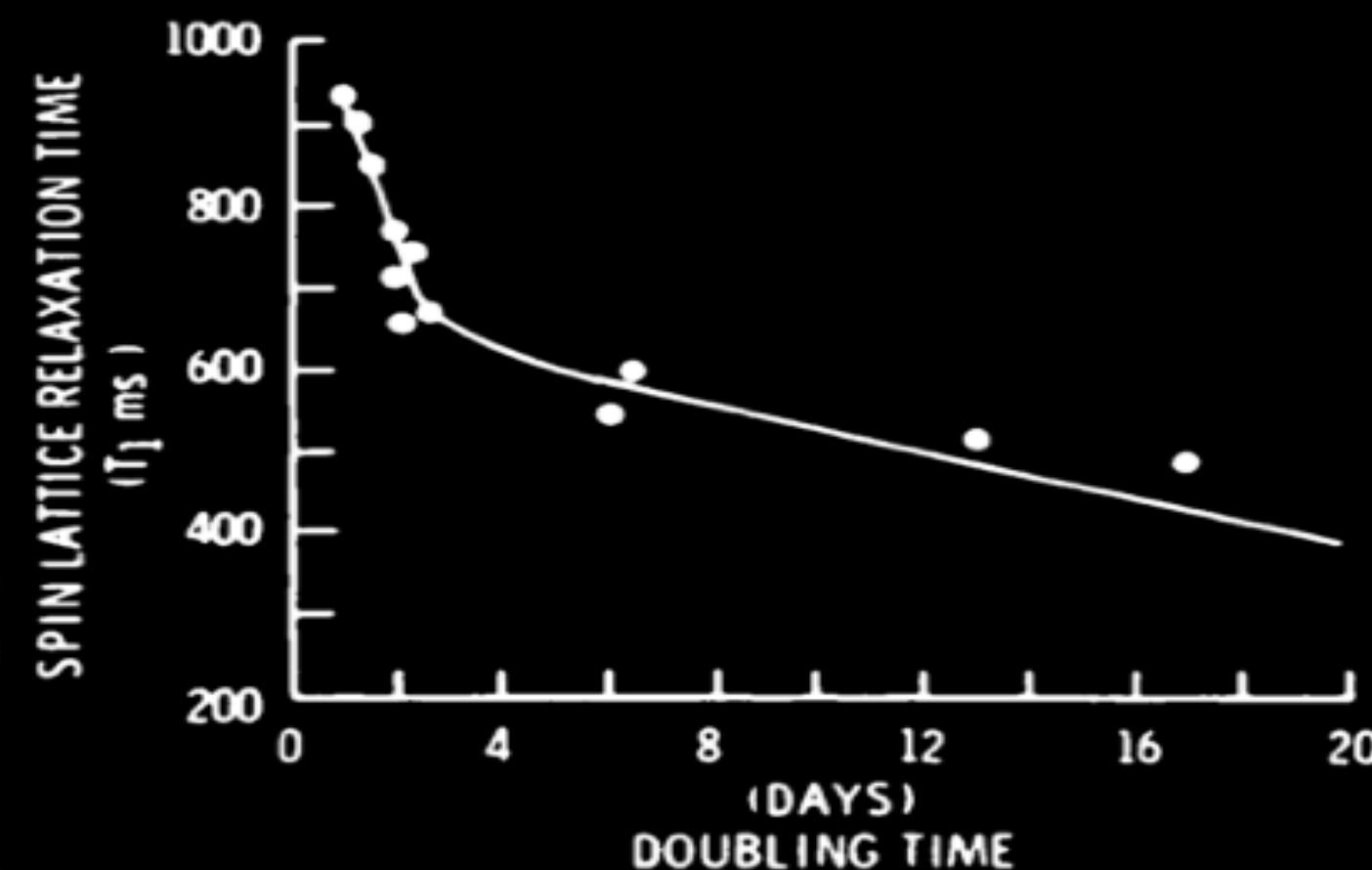
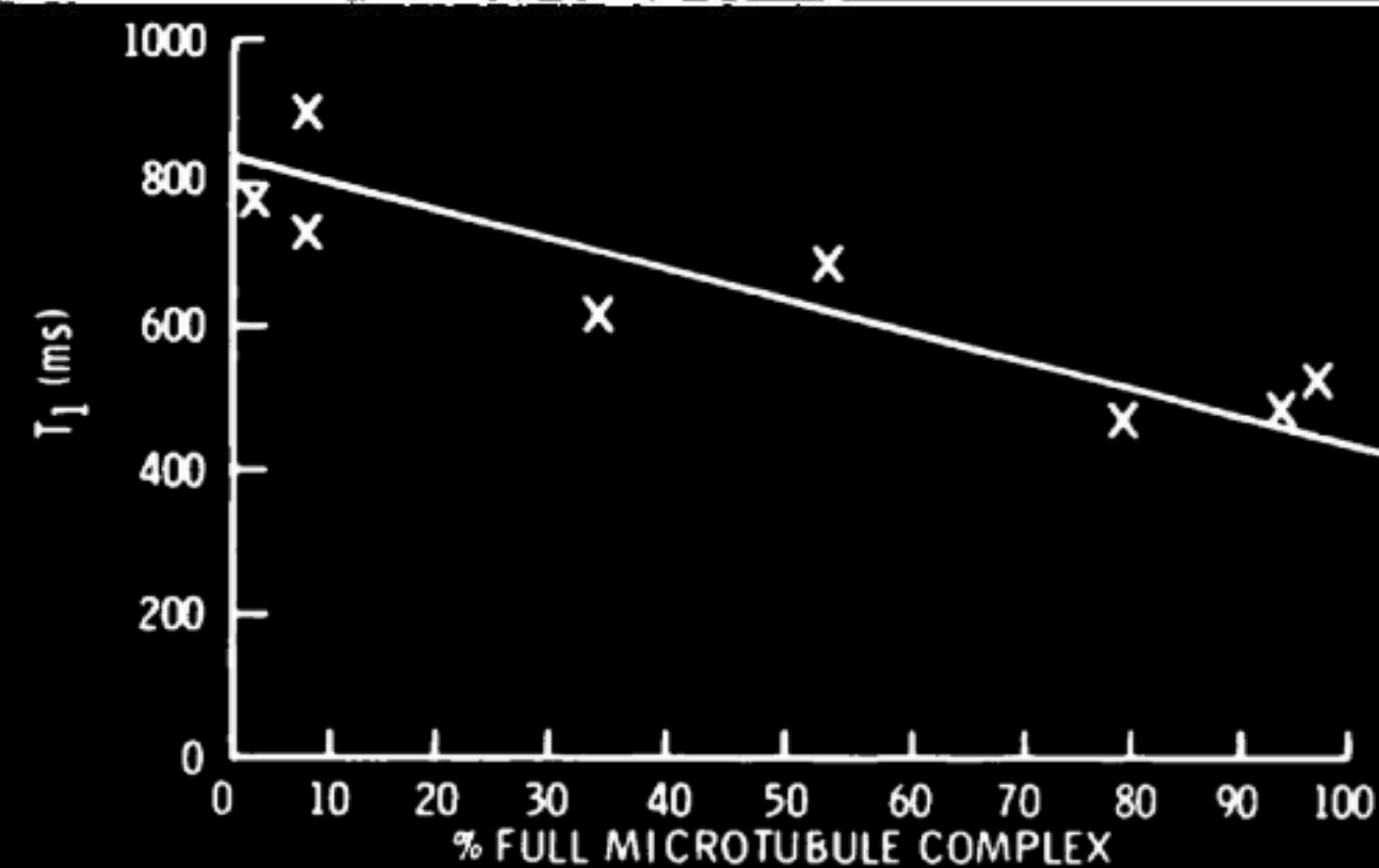
$$y = \log(\text{glucose\_uptake})$$
$$x = \text{water polarity}$$



FUN FACT: 10% DMSO increases solvent polarity measurement (GP + 0.2) and subsequently decreased glucose uptake by 60+% on preliminary internal trials

Water polarity is proportional to growth rate in cancer cells. Water polarity, under NMR (MRI), is proportional to microtubule content. Microtubules have a high surface area in cells and may polarize the majority of cell water in slow-growing cells. Microtubules have a disordered C-terminal domain which can either adsorb ions or fold onto the rest of the microtubule. Microtubules have been shown to exhibit memristive properties at the sub-cellular level. Adsorption and desorption of ions alter the surface potential, creating an ion-dependent voltage. The  $pK_a$  of negatively charged carboxyl groups is affected by the desorption kinetics. This is predicted by the Debye-Hückel equation. Disordered proteins are seen to have exposed hydrophobic backbone, polarizing and orienting water molecules. If either folded into tubulin monomers or folded into microtubules, the water is depolarized, as the part

## Target Microtubules, Read water.



### Microtubule Complexes Correlated with Growth Relaxation Times in Human Breast Cancer Cells<sup>1</sup>

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#### ABSTRACT

Ten established human breast cancer cell lines display patterns of microtubule organization which are characterized by growth rate of the cell populations and the freedom of mobility of cellular water molecules measured by nuclear magnetic resonance spectroscopy. Cell lines with population-doubling times of 1 to 2 days demonstrate rapid mobility of water molecules by proton spin-lattice and spin-spin relaxation times ( $T_1 > 750$  msec,  $T_2 > 120$  msec) and have diffuse patterns of tubulin immunofluorescent antibody staining. Moderately fast dividing cells (population-doubling times of 3 to 7 days) have  $T_1$  values of 600 to 750 msec and show approximately 50% organized complexes of polymerized microtubules in the cytoplasm. Slow-growing cell lines demonstrate more restricted mobility of water molecules ( $T_1$  values of 500 to 600 msec) and contain abundant networks of polymerized microtubules. The three-way correlation of the physical parameter of water proton relaxation times, the structural parameter of microtubule organization, and the physiological parameter of growth suggest a close interaction of water molecules with the cytoplasmic macromolecular network in the performance of physiological function.

motional freedom, due to interactions with surfaces.

If relaxation times of water protons accurately reflect the average motional freedom of water molecules in cells, then the apparent reduced motion of cytoplasmic water and alterations in its solvent properties could lead to the alteration of the rates of many physiological functions such as metabolite diffusion, enzyme-hydrogen donor kinetics, and ion solubility. Such changes may account for a general reduction in cellular doubling time that would correlate with  $T_1$  values and be related to cytoplasmic macromolecular organization.

The results presented in this paper are not to be taken as a