Redox-Active Artificial Molecular Carriers for Ion Transport Across Cell Membranes

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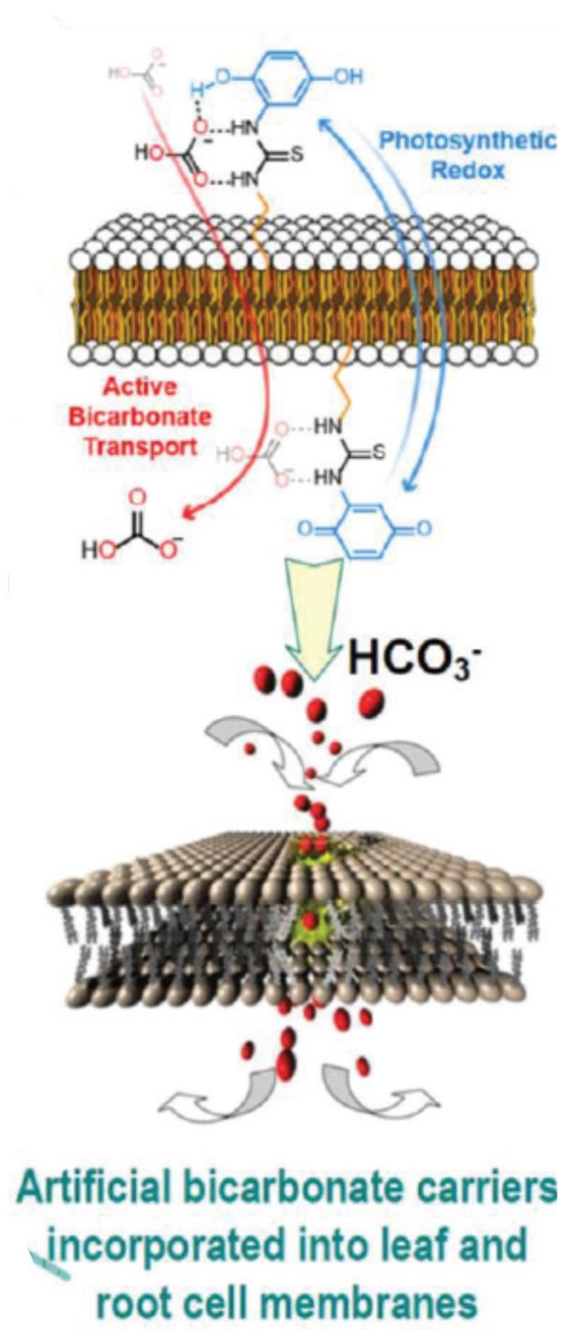
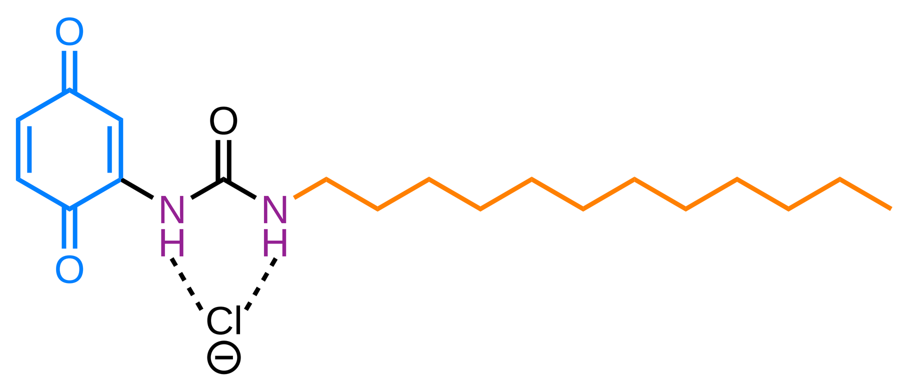
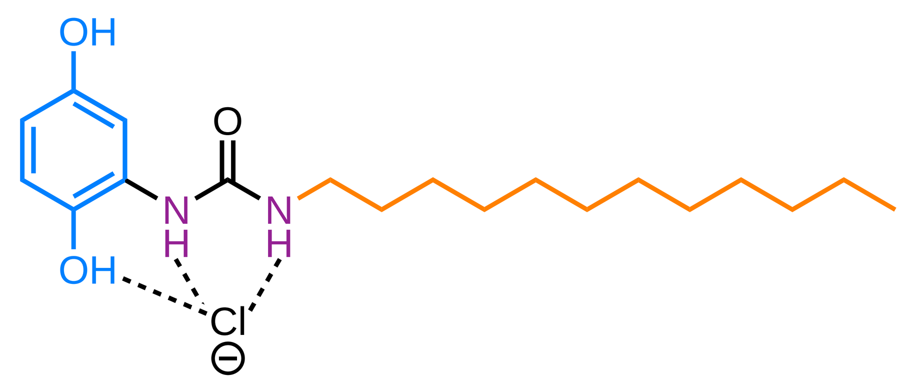


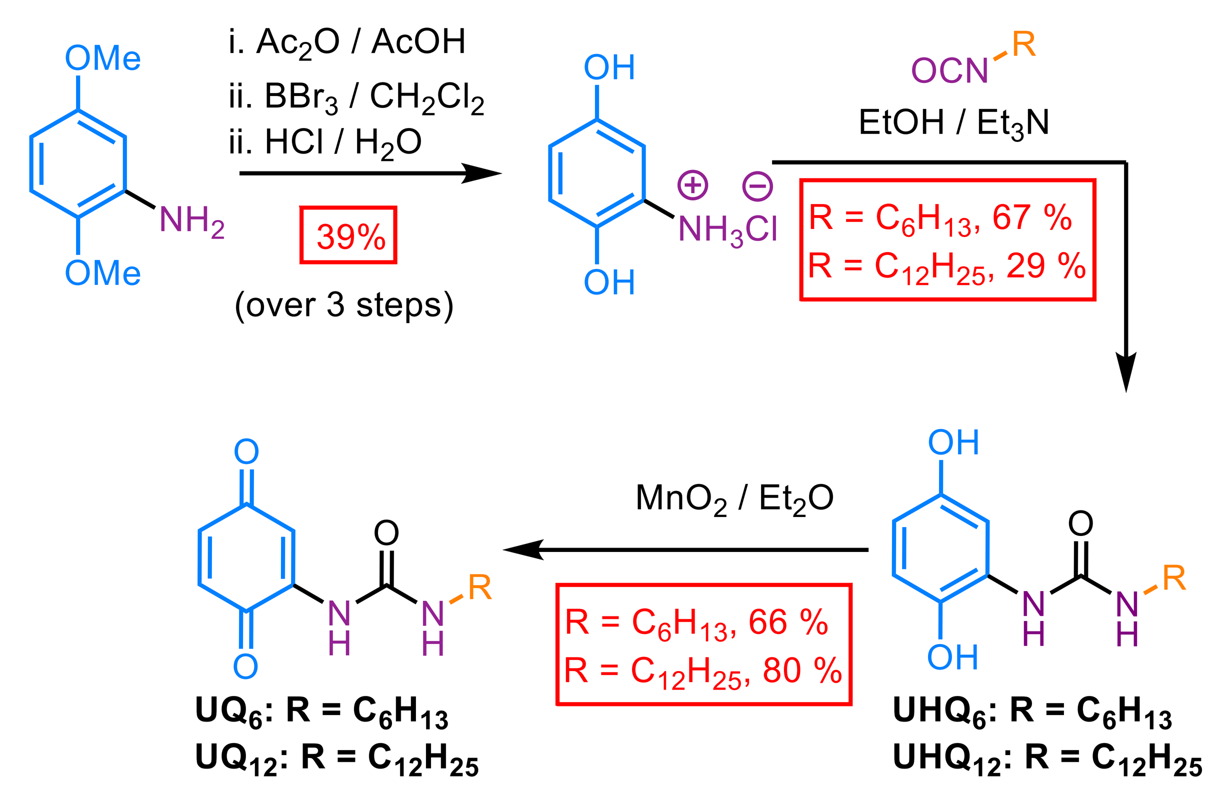
Introduction & Project Aims

- In biological systems: transmembrane ion transport is facilitated by membrane-embedded **ion channels** and **pumps**
- Synthetic transmembrane anion transporters have direct applications in medicinal chemistry as potential **cystic fibrosis** and **cancer treatment**
- A vast array of anion transporters have been reported, but none have demonstrated an ability for **active transport**
- Active transport: "**uphill**" movement of ions from an area of low concentration to an area of high concentration; an **entropically unfavorable** process that requires a **fuel**
- To synthesize **urea** and **acyl urea**-based chloride ion transporters with a **redox-active** quinone/hydroquinone motif, capable of facilitating the active transport of **chloride ions**





Urea-based Ion Transporters



Scheme 1: Synthesis of urea transporters.

Vesicle Preparation for Ion Monitoring

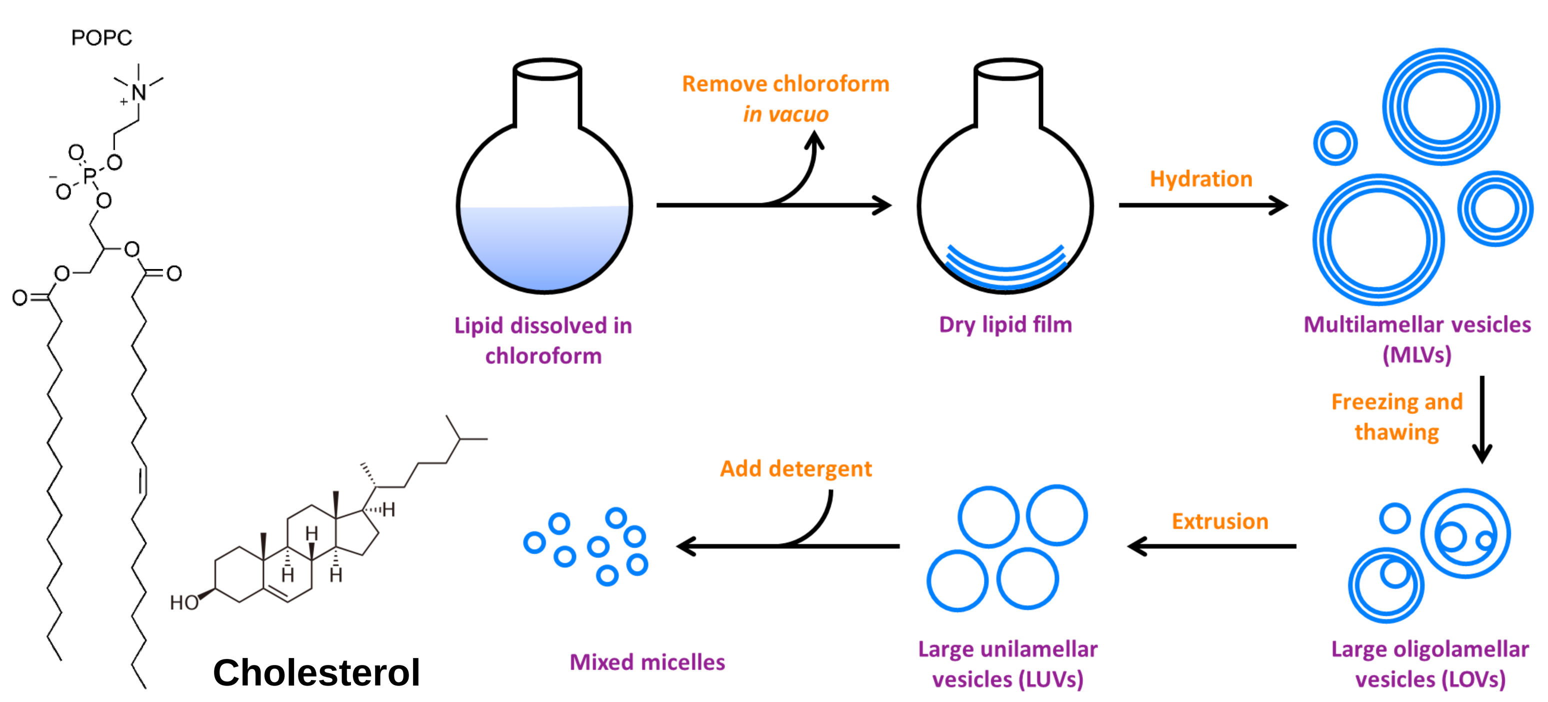


Figure 1: Preparation of vesicles for transport experiments using POPC and Cholesterol Lipids

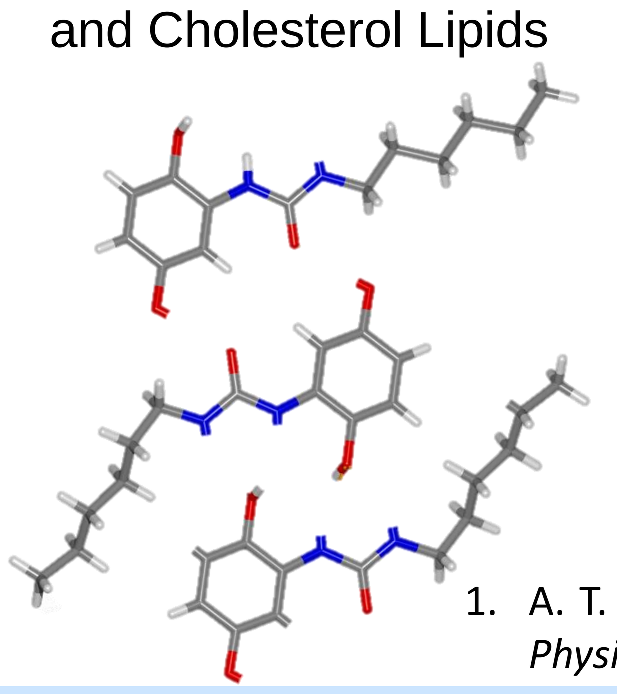


Figure 2: single crystal of a urea transporter has also given us insights into its hydrogen bonding properties. The solid-state structure reveals hydrogen bonding interactions between the neighbouring urea and hydroquinone units.

Passive Ion Transport Experiments

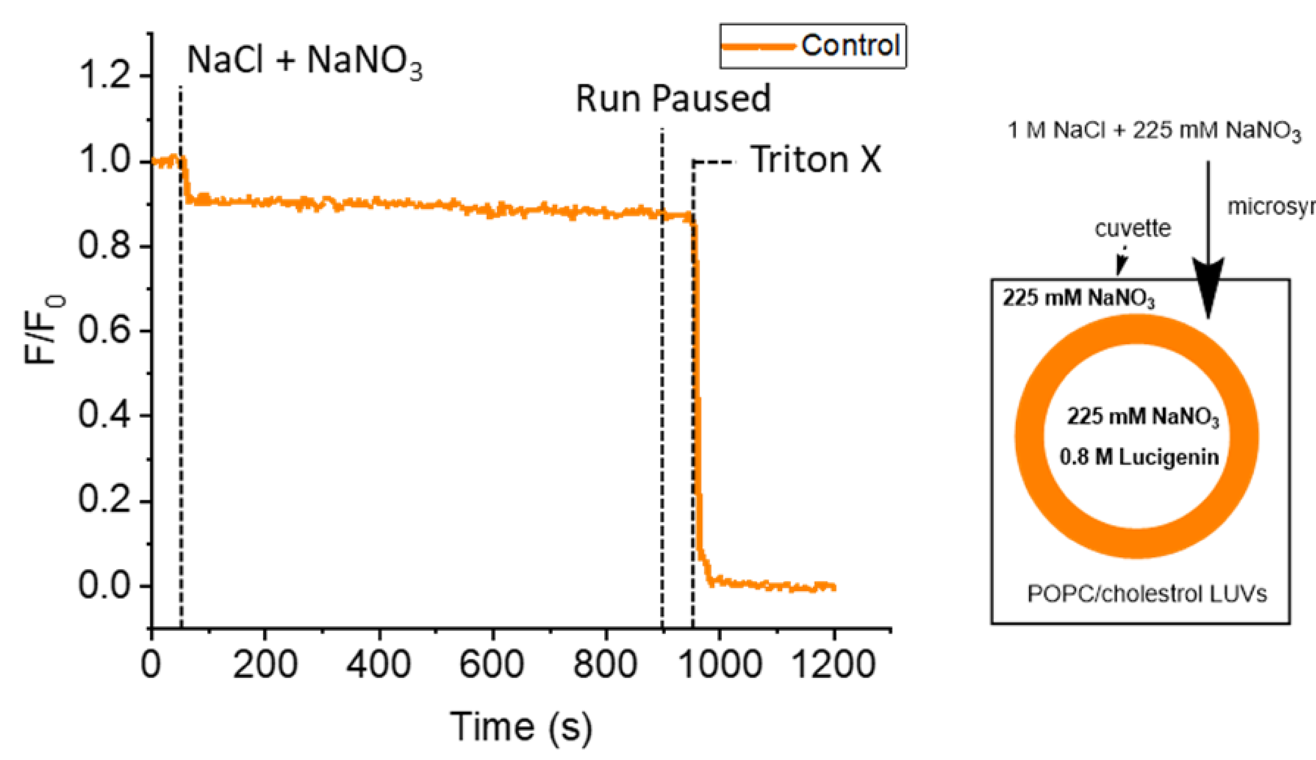


Figure 3: Passive ion transport experiment for measuring ion transport capability in transmembrane

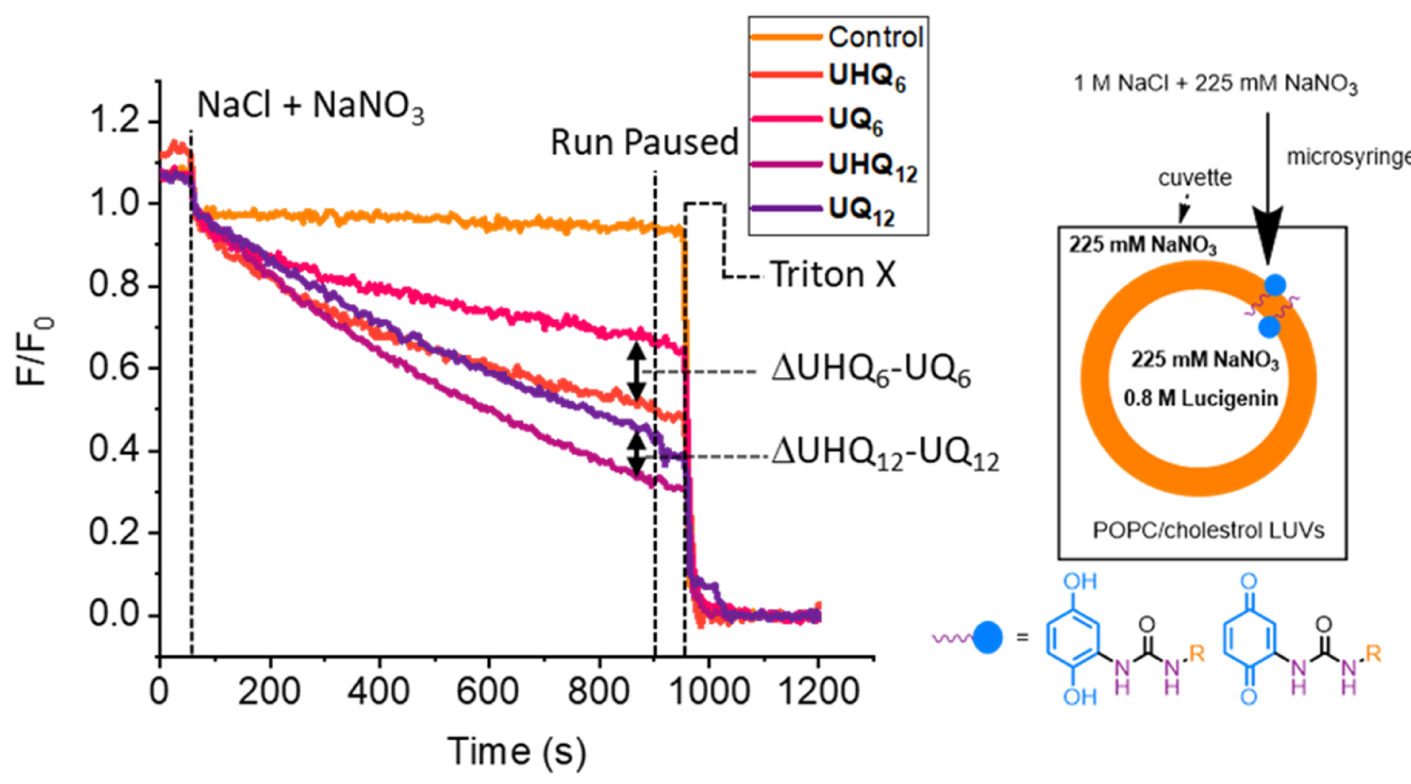


Figure 4: Fluorescence decay of lucigenin caused by the influx of Cl^- into 200 nm LUVs consisting of 7:3 POPC:cholesterol (0.4 mM lipid concentration in 225 mM $NaNO_3$), with preincorporated hydroquinones RABCs (**UHQ_6** & **UHQ_{12}**) and quinones RABCs (**UQ_6 & UQ_{12}**) at 5 mol% loading w.r.t. lipid concentrationFluorescence of Lucingenin in HQ Gen 4 vesicles over 15 min. Cl- solution was added at 1 min (225 mM $NaNO_3$ + 1M NaCl, 50 uL).

Summary

A family of urea based ion transporters have been synthesized with suitable binding constant for ion transport across membranes. Preliminary results show using artificial cells (vesicles) have shown that ion transport of Cl- ions across membranes happens readily.

1. A. T. Wilson and M. Calvin, *J. Am. Chem. Soc*, 1953, **77**, 5948. 2. T. D. Sharkey, *Physiol. Plant.*, 1988, **73**, 146–152. 3. H. P. Kortschak, C. E. Hartt and G. O. Burr, *Plant Physiol.*, 1965, **40**, 209– 213.