Cationic surfactants are key ingredients in many household & personal care products, biocides & industrial processes.

- $K_{OW}$ not possible/available for “ionized surfactants”, hampering chemical fate & environmental risk assessments.
- Partitioning of ionic surfactants into phospholipid membranes ($K_{MW}$) likely dominates in organismal tissue.
- Using two “updated” phospholipid-based assays (ref A+B), measured $K_{MW}$ for 19 surfactants show surprising series.
- Bilayer membrane data calibrated simple $K_{MW}$ models. $K_{MW}$ is used (besides $K_{OW}$) in a bioaccumulation model (ref C).

### Measuring and Modeling Membrane-Water Partitioning Coefficients for Cationic Surfactants

#### Q1: measuring $K_{MW}$ ?

2 METHODS:

- **Solid-Supported Lipid Membrane**
  (SSLM, “TRANSIL” non-covalently linked bilayer)
  
  SSLM leak 1% of phospholipids: effect if $K_{MW} > 4$ ! (ref A)
  
  Modified SSLM protocol: in 2mL HPLC vials + PBS renewal
  
  Measurements become difficult if $>C_{14}$ ($K_{MW} > 6$)
  
  $K_{MW}$ increase with alkyl chain & RN-H$_3$ > RN-H$_2$ > RN-H > RN-$^+$

- **Immobile Artificial Membrane HPLC**
  (IAM-HPLC, bound monolayer coating)
  
  Eluent @ pH5 to minimize confounding electrostatics (ref B)
  
  $K_{MW}(IAM) = 18.9 \cdot k_{IAM}$; use solvent series up to $K_{MW}$ of 6

### CATIONIC SURFACANTS:

- 19 chemicals (pK$_a$ > 9.5), C$_{6-14}$ alkyl chain (R), 7 head group types

<table>
<thead>
<tr>
<th>SSLM</th>
<th>$K_{MW}$ (log)</th>
<th>H$_3$</th>
<th>H$_2$</th>
<th>H$_1$</th>
<th>N$^+$</th>
<th>Benz</th>
<th>Pyr</th>
<th>R$_2$</th>
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</thead>
<tbody>
<tr>
<td>C$_6$</td>
<td>2.1</td>
<td>3.1</td>
<td>2.8</td>
<td>2.4</td>
<td>2.2</td>
<td>2.1</td>
<td>3.1</td>
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<tr>
<td>C$_8$</td>
<td>4.7</td>
<td>4.0</td>
<td>3.7</td>
<td>3.3</td>
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<tr>
<td>C$_{10}$</td>
<td>5.3</td>
<td>5.3</td>
<td>5.4</td>
<td>5.6</td>
<td>5.3</td>
<td>5.3</td>
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<tr>
<td>C$_{12}$</td>
<td>4.9</td>
<td>4.9</td>
<td>5.4</td>
<td>5.6</td>
<td>5.3</td>
<td>5.4</td>
<td>5.6</td>
<td></td>
</tr>
</tbody>
</table>

#### Q2: modeling $K_{MW}$ ?

- **QSAR based on SSLM data**, with correction factors if head is not N-H$_3$ (not for N-R$_2$ & N-Pyr):

  \[
  \log K_{MW} = -1.6 + 0.59 \cdot R - 0.28 \ (if \ N^+H_2) - 0.56 \ (if \ N^+H) - 1.1 (if \ N^+) - 0.1 (if \ N^+Benz)
  \]

- **QSAR based on IAM-HPLC data**, with two amine type correction factors, for pH 7.4:

  \[
  \log K_{MW} = \log K_{MW(IAM-PH5)} + 0.8 \ (if \ N^+H_3) + 0.5 \ (if \ N^+H_2)
  \]

- **COSMOmic simulation**: 3D hydrated lipid bilayer (MD) & quantum chemistry-optimized 3D input structures

  \[
  \log K_{MW} = \log K_{DNPCW(TUHH)} - 0.17 (if \ N^+H_3) + 0.3 (other)
  \]