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Mimicking Nature – Imitating Ion Carriers Using Crown Ethers in a Vertical Pressman Cell

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Abstract Valinomycin, an antibiotic ionophore (ion carrier), is a functional analog of the cyclic hexaether [18] crown-6 (18C6). Both valinomycin and 18C6 molecules form lipophilic complexes with alkali metal ions. Hence, upon addition of valinomycin or 18C6, alkali metal salts become soluble in non-polar organic solvents. The ability to complex cations allows valinomycin molecules to transport these ions across cell membranes. Since 18C6 molecules bind alkali metal cations in a similar way, by wrapping them in a "greasy coat", cell transport processes by valinomycin can be imitated using the more cost-efficient and less hazardous 18C6. In a simple test tube experiment, cell conditions are mimicked by means of a triphasic system consisting of an aqueous magnesium sulfate ($MgSO_4$) solution (bottom phase) and an aqueous potassium permanganate ($KMnO_4$) solution (top phase) which are separated by a methyl benzoate phase serving as a liquid membrane. If a solution of 18C6 is injected into the methyl benzoate phase of this "vertical PRESSMAN cell", a salt transfer from the upper aqueous phase to the bottom phase can be observed, modelling the effect of valinomycin in living cells. Appropriate simplifications for use in schools are discussed and animations are provided to illustrate the ionophore-facilitated cell transport.

Keywords: *high school, organic chemistry, hands-on learning, crown ethers, ionophores/ ion carriers, membranes*

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1. Introduction

1.1. Crown Ethers

The ability of macrocyclic polyethers with the formula $(-CH_2-CH_2-O-)_n$ to selectively bind alkali metal cations in their ring interior (cavity [1]) was first recognized by Charles PEDERSEN in the early 1960s [2]: More or less accidentally [3], he synthesized the cyclic hexaether 1 (see Figure 1), in the presence of which sodium hydroxide (NaOH) could be dissolved in methanol. PEDERSEN recognized that a sodium ion can be bound in the molecule's cavity, i.e. that it can form the complex $1{\cdot}Na^+$ (see Figure 1) [2]:

"It seemed clear to me now that the sodium ion has fallen into the hole in the centre of the molecule and was held there by the electrostatic attraction between its positive charge and the negative dipolar charge on the six oxygen atoms symmetrically arranged around it in the polyether ring."[2, p. 1024]

Later, it was discovered that also other alkali and alkaline earth metal cations are complexed by 1 and other cyclic polyethers. The stability of the corresponding complexes is controlled, among other factors, by the size ratio of the cavity to the ion diameter: cations that fit particularly well into the crown cavity are bound strongest, which allows selective cation binding by crown ether molecules [2,4].

Due to the similarity of the polyethers' molecular models to a royal crown (see compound 2, Figure 1, cf. [5]), PEDERSEN referred to this new class of compounds as *crowns [2]*. Later on, these compounds were named *crown ethers* to clarify the chemical class [6,7]. PEDERSEN developed a simple nomenclature system in which the number of ring atoms is given first in square brackets, followed by the name *crown* and finally the number of oxygen atoms. Accordingly, compound 2 is named [18] crown-6 (18C6). Additional substituents are placed in front of the macrocycle's name, as the example of dibenzo [18] crown-6 (DB18C6) (1) illustrates (In this example, two additional benzene rings are formally fused to the 18C6 molecule). PEDERSEN's nomenclature has become established among experts to this day due to its simplicity [2,4,6].

The discovery of the complexation of alkali metal cations by crown ethers was of particular significance: Until the early 1960s, no (*synthetic*) compounds were known that could bind the "hitherto recalcitrant alkali cations [2]." (In fact, crown ethers and crown ether-like macrocyclic polyethers were already known before

PEDERSEN's discovery. However, their potential to bind alkali metal cations was recognized by PEDERSEN for the first time [2,3]).

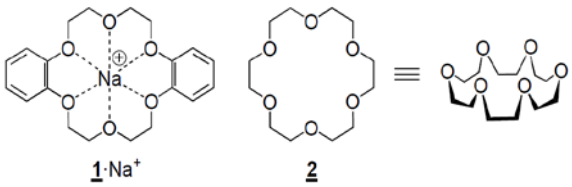

Figure 1. Lewis structure of Na(DB18C6)$^+$ (**1**·Na$^+$) and 18C6 (**2**) and illustration of its resemblance to a royal crown

Donald CRAM and Jean-Marie LEHN continued PEDERSEN's work and created further macrocyclic polyethers such as the so-called cryptands, e.g. 3, and the spherands, e.g. 4, which could even better complex alkali metal cations [5,8]. In 1987, PEDERSEN, CRAM and LEHN were awarded the Nobel Prize in Chemistry "*for their development and use of molecules with structure-specific interactions of high selectivity* [9]." The Nobel Prize is said to mark (more or less) the beginning of *supramolecular chemistry* [3,7], which is the chemistry beyond (lat. *supra*) the molecule [7,10], dealing with interactions between molecules and/ or ions [11].

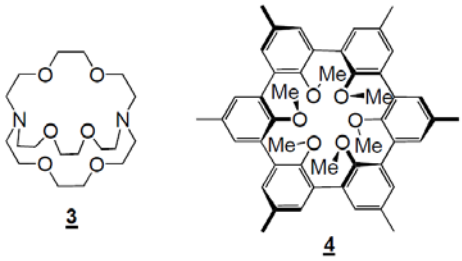

Figure 2. A cryptand (3) and a spherand (4) synthesized by CRAM and LEHN

Supramolecular interactions are found in abundance in nature, e.g. in enzyme – substrate complexes, antigen–antibody interactions and ion carrier–ion interactions [10]. Usually, the larger molecule that binds a smaller molecular or ionic component is referred to as the "*host*" and the smaller one as the "*guest*". Accordingly, supramolecular aggregates ("*supermolecules*") are often called "*host – guest complexes*" [10,11].

1.2. Ionophores (Ion Carriers)

A well-studied ionophore (ion carrier) is valinomycin [12]. It was first isolated in 1955 from a strain of actinomycete belonging to the species *Streptomyces fulvissimus*. Valinomycin is a natural antibiotic that is, for example, effective against *mycobacterium tuberculosis*, the bacterium that causes tuberculosis [13].

In 1967, PRESSMAN et al. recognized that valinomycin molecules (5) are capable of complexing and transporting alkali metal cations across cell membranes as lipophilic and therefore fat-soluble complexes. Due to this property, PRESSMAN et al. called valinomycin and related compounds ionophores ("ion carriers") [14,15,16]. In fact, this very property makes valinomycin an antibiotic: Valinomycin molecules bind biologically relevant potassium ions in their hydrophilic cavity (5·K$^+$) with the methyl and isopropyl groups attached to the cycle directed outwards [16,17].

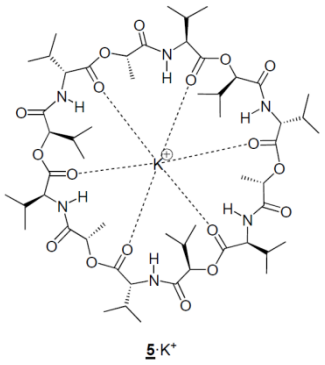

Figure 3. Lewis structure of the K(valinomycin)$^+$ complex

The resulting hydrophobic surface of the valinomycin molecule lipophilizes the enclosed cation, i.e. makes it fat-soluble [16]. Corresponding lipophilic complexes are then able to penetrate the lipid membrane of a variety of different cells such as bacterial, virus and mammalian cells [12,16].

This way, potassium ions can be transported from the aqueous cell exterior through the cell membrane and be released ("decomplexation") into the aqueous cell interior *increasing* the potassium ion concentration within the cell. Conversely, potassium ions can be transported out of the aqueous cell interior and *reduce* the potassium concentration inside the cell (usually in bacterial cells). Either way, the ion transport disrupts the cell's sensitive potassium ion balance, which ultimately leads to cell death [12,16,18]. The ionophore-facilitated cation transport processes are illustrated in Figure 4 (cf. [16]).

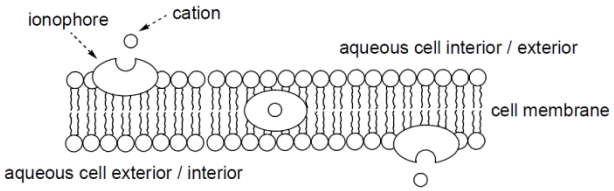

Figure 4. Cation transport out of or into a cell, facilitated by an ionophore molecule (e.g. valinomycin)

2. Biomimetic Imitation of Ionophores using Crown Ethers

The similarity between crown ethers and natural ionophores such as valinomycin was quickly recognized [7,19]: Just like the natural ionophores, crown ethers bind alkali metal cations in their hydrophilic interior. With the hydrophobic ethylene groups (-CH_2-CH_2-) facing outwards lipophilic complexes are formed (cf. Figure 5) [1].

The resemblance between 18C6 and valinomycin becomes particularly evident when examining the crystal structure of the valinomycin molecule – potassium ion complex: Figure 6 shows a top view of the crystal structure of 5·K$^+$, taken from [20].

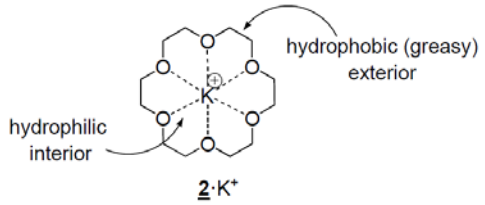

Figure 5. Encapsulation of a K^+ ion by a 18C6 molecule, cf. [1]

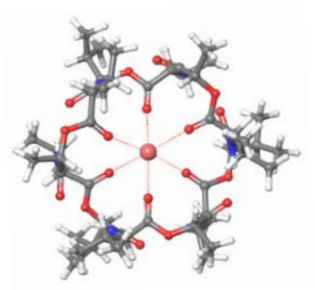

Figure 6. top view of the crystal structure of $\underline{5}\cdot K^+$, taken from [20]

PEDERSEN's discovery of crown ethers was of particular importance for biology [2,19], as the mode of action of valinomycin and other related natural antibiotic ionophores could now be imitated using crown ethers as model compounds and thus be better understood [21]. The scientific community drew great benefit from this, and chemistry education also recognized the potential of imitating cell membrane transport processes using crown ethers, especially 18C6 and DB18C6 [22].

2.1. Preliminary Work on the Imitation of Cell Transport Processes

2.1.1. Prior research

Different cations (M^{n+}) are transported through cell membranes to different degrees (i.e. selectively) by valinomycin or ionophore molecules (ip) in general [14]. How effective the cation transport ultimately is, depends in particular on the equilibrium constants *K* of the complexation *within* the cell membrane (equation 1) [23].

$$M^{n+} + ip \rightleftharpoons M(ip)^{n+} \quad K = \frac{c\left(M(ip)^{n+}\right)}{c\left(M^{n+}\right)c(ip)} \qquad (1)$$

As noted by PRESSMAN [14,24], in the ionophore-facilitated extraction of alkali metal salts from water into an organic phase, the same selectivity sequences can *generally* be observed as in ionophore-facilitated alkali ion transport through mitochondrial cell membranes. Thus, in order to make predictions about how well various ionophores bind alkali metal cations in biological membranes and transport them across them, simple metal salt liquid-liquid extraction experiments can be carried out with the corresponding ionophores. In these experiments, the organic phase serves as a model lipid membrane [24].

In 1970, ASHTON and STEINRAUF [25] developed an experiment using a liquid membrane that illustrates the ionophore-facilitated transport of cations from the aqueous cell exterior into the aqueous cell interior (or vice versa) particularly well. The corresponding experimental setup involved a U-tube containing chloroform ($CHCl_3$) as a model membrane in which the ionophores to be studied were dissolved (Figure 7). This chloroform solution was layered on one side of the U-tube with an aqueous alkali metal salt solution ("*donor phase*") and on the other with water ("*receiving phase*"). Once the alkali metal cations were bound by the ionophore molecules, they became soluble in the chloroform phase. Due to charge compensation, the corresponding anions (A^-) remained associated with the positive ionophore complexes ($M(ip)^{n+}$) and followed them through the liquid phase. Over time, the salts were thus transported from the donor phase to the receiving phase until the concentration difference was compensated [25,26]. The reader may compare this setup (Figure 4) with the cation transport processes in living cell shown in Figure 7.

If in the experimental setup of ASHTON und STEINRAUF metal picrates (salts of the toxic and in dry form explosive picric acid, i.e. 2,4,6-trinitrophenol (TNP)) are used that form yellow solutions, the process can be observed with the *naked eye*. In order to accelerate the process of ion transport, ASHTON and STEINRAUF stirred the chloroform phase continuously [25].

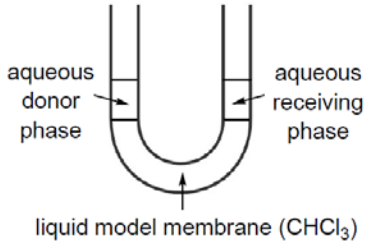

Figure 7. U-tube experiment by ASHTON und STEINRAUF for modelling and studying the ionophore-facilitated cation transport across cell membranes

The driving force behind the transfer of a binary salt MA (= cation M^+, anion A^-) from one side of the U-tube to the other is the concentration gradient or, to be more specifically, the difference in chemical potential of the salts (μ_{MA}) in the aqueous phases connected by the organic phase at the start of the experiment (equation 2):

$$\mu_{MA,left} \neq \mu_{MA,right} \qquad (2)$$

The transport takes place until a so-called DONNAN equilibrium is established in which the chemical potentials (i.e. the concentrations c_{MA}) are the same on both sides. In this case, equation (3) applies [25, 27].

$$c_{M^+,left} \cdot c_{A^-,left} = c_{M^+,right} \cdot c_{A^-,right} \qquad (3)$$

Another way to generate a system with a liquid membrane separated by two aqueous phases in a vertical setup was developed by PRESSMAN and DE GUZMANN in 1974 (Figure 8) [28]. They placed an aqueous 30 % sucrose solution in a flat-bottomed tube, overlaid it with a binary solvent mixture of CCl_4 (39 vol.%) and decane (61 vol.%) containing the ionophore to be studied, and overlaid this solution with water. The sucrose in the bottom aqueous phase only serves to increase the density of this solution so that it can be easily overlaid with the CCl_4/decane mixture, which in turn can be easily overlaid

with water due its lower density. Upon the addition of a suitable alkali metal salt – they used radioactively labelled metal cations – a salt transport through the liquid membrane was observed. For more details, see [28].

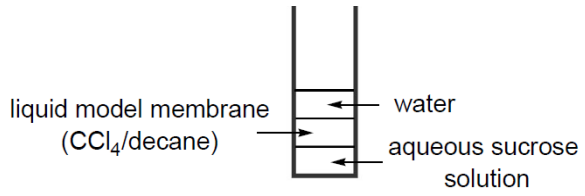

Figure 8. Vertical setup by PRESSMAN and DE GUZMANN to model and study the ionophore-facilitated cation transport across cell membranes

Not only natural ionophores can be used in these types of experiments. Synthetic alkali metal cation binders such as cryptands [29] or crown ethers [30] also transport suitable salts through model liquid membranes. Today, setups consisting of a liquid membrane separated by two aqueous phases are generally termed PRESSMAN cells [26].

2.1.2. Prior Work in the Field of Chemistry Education

Due to its antibiotic properties, valinomycin is toxic and also relatively expensive [31]. By contrast, 18C6 or DB18C6 are neither harmful nor toxic, but have similar membrane transport properties as *natural* ionophores [26]. Please note that crown ethers were regarded as toxic for a long time. However, toxicological studies have shown that toxicity issues are largely a myth [3]. Furthermore, crown ethers are relatively inexpensive and can therefore serve as valinomycin mimics in school teaching.

In 1980, MONDEN et al. [17] adopted the U-tube experiment developed by ASHTON and STEINRAUF as a school experiment to model the permeation of ions through cell membranes. They used chloroform as a liquid membrane and 18C6 as the ionophore instead of valinomycin. In this way, they showed that both potassium picrate and potassium permanganate ($KMnO_4$) could be transported through the chloroform phase from one side of the U-tube to the other.

In 2013, FRIEDRICH and OETKEN replaced chloroform with the more school-suitable dichloromethane (CH_2Cl_2, DCM). They also used the U-tube setup of ASHTON and STEINRAUF to demonstrate the transport of $KMnO_4$, potassium hydrogen chromate ($KHCrO_4$), potassium iodide (KI) and sodium permanganate ($NaMnO_4$) with the help of 18C6 or [15]crown-5 (15C5) [32].

We have developed a low-cost U-tube in a TicTac® box to demonstrate ionophore-facilitated permeation of cations across cell membranes [33]. To turn a TicTac® box into a U-tube, an array of 2x2 hot glue sticks (diameter 11 cm) glued together was inserted into the box in such a way that a square U-shaped gap was created (see Figure 9). Since the glue stick array was a little too large for the TicTac® box, it bulged the box slightly, thus ensuring that the construction was tight. When this "PRESSMAN cell" was filled with a solvent, it could therefore not get between the glue sticks and the TicTac® wall.

Instead of DCM, which is harmful to health, we used benzoic acid methyl ester ("methyl benzoate") as a liquid membrane. This solvent is used in personal care products such as shampoo and cosmetics both due to its sweet, floral odor and its preservative properties [34], and can therefore be used in schools without any problems. Moreover, methyl benzoate (ϱ = 1.08 gml^{-1}) has a higher density than water and can therefore be easily overlaid with water in the same way as chlorinated solvents. After adding methyl benzoate to this low-cost U-tube, a small magnetic rod was inserted to stir the organic phase. One arm of the cell was then filled with a 0.1 M aqueous $KMnO_4$ solution and the other with water. If 1 mL of a 0.4 M solution of 18C6 in methyl benzoate is injected into the methyl benzoate phase of this low-cost U-tube, a transfer of $KMnO_4$ from one aqueous phase to the other was observed within 1-2 minutes [33]. By contrast, experiments in conventional U-tubes typically take up to 30 minutes [32].

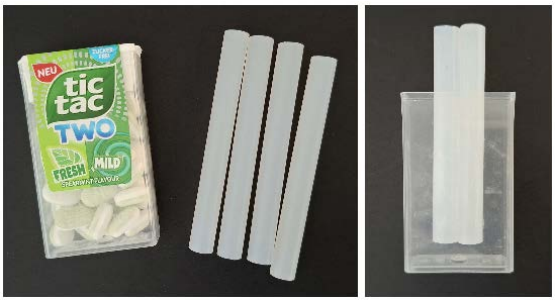

Figure 9. low-cost U-tube made from a TicTac® box and glue sticks

Altogether, the proposed experimental setup in a TicTac® box meets the requirements of chemistry education to work with small quantities in order to reduce hazards and to replace expensive (glass) devices with other devices such as disposable syringes – this often makes it possible to use this kind of setups in student experiments [35]. The short duration of the experiment also makes the "TicTac® U-tube" particularly suitable for school applications. Overall, the experiment proposed fulfils all the '*low* criteria' for a school experiment introduced by BANERJI, namely that it is cost-effective (*low cost*), involves little risk (*low risk*), can be implemented quickly (*low time*) and without high technical requirements (*low tech*) [33,36].

2.2. Developing a New Vertical PRESSMAN Cell for the Use in Schools

As described in section 2.1, model experiments on ionophore-mediated cation transport across cell membranes have always relied on the use of a U-tube or, recently, on the use of a low-cost U-tube from a TicTac® box for the use in schools. As will be shown below, following the example of PRESSMAN's vertical setup, ion transport can also be modelled in a simple *test tube experiment*. This completely eliminates the need to use an expensive U-tube or to build a low-cost U-tube. Importantly, the test tube experiment allows demonstrating complexation and decomplexation separately and in combination. In our previous publication [33], solvent and crown ether were switched during this step-by-step modelling: first the complexation of potassium ions was demonstrated by dissolving $KMnO_4$ in anisole with 18C6, then a solution of K(DB18C6)MnO_4 in anisole underlaid with water was used to show

decomplexation and finally, for the combination of both processes in a TicTac® box, 18C6 was applied to show the transport of $KMnO_4$ across methyl benzoate (see above). This may raise the question for learners as to why or whether the change of solvents and crown ethers are relevant. It is therefore proposed to demonstrate the transport of ions through cells in model experiments using methyl benzoate and 18C6 *alone*, i.e. to show both complexation and decomplexation using only these two components besides $KMnO_4$.

2.2.1. Complexation

The first step in both the (natural) ionophore-facilitated cation transport across biomembranes and the crown ether-facilitated cation transport across liquid model membranes is the complexation of the cation. To demonstrate this step, 2.5 mL of methyl benzoate (= model membrane) is overlaid with 1.5 mL of an aqueous 0.1 M $KMnO_4$ solution. In this way, a two-phase system is formed in which the intensively colored potassium permanganate salt remains in the aqueous phase (model for the aqueous cell exterior/ interior) due to the absence of an ionophore. Consequently, the organic phase (model for the lipid membrane) remains colorless (Figure 10, left). Using a 1 mL syringe with a needle, 0.5 mL of a freshly prepared 0.3 M solution of 18C6 in methyl benzoate is then injected into the organic phase of the two-phase system just below the phase boundary. After this addition, the methyl benzoate phase turns violet (Figure 10, middle and right) since 18C6 molecules bind potassium ions and transfer them to the organic phase. This complexation is *indirectly* (!) visible by the co-transport of the permanganate anions.

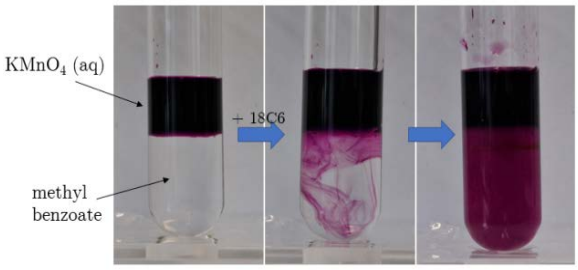

Figure 10. Complexation: $KMnO_4$ transfer from water to methyl benzoate upon addition of 18C6 (takes less than a minute)

For comparison, Figure 11 shows a scheme of the corresponding *biological process* (see Figure 4) that the experiment aims to mimic.

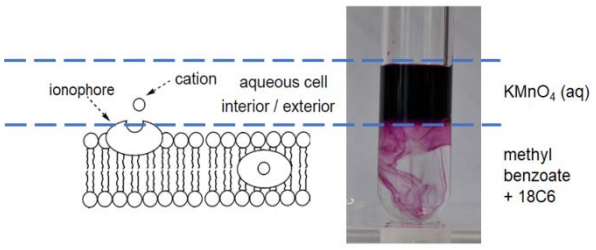

Figure 11. Comparison of the test tube experiment modelling complexation of potassium ions by an ionophore at/ near the cell membrane

The process can be visualized at the particle level as shown in Figure 12a-c.

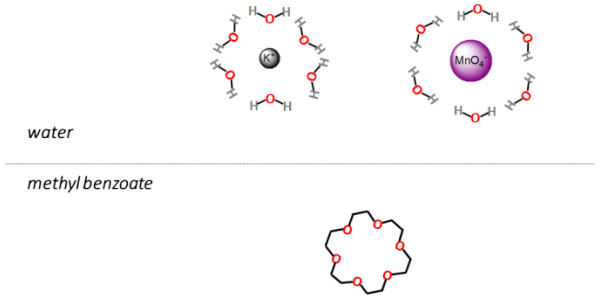

Figure 12a. Complexation at particle level: $KMnO_4$ dissolved in water, complete hydration, underlying methyl benzoate phase with 18C6

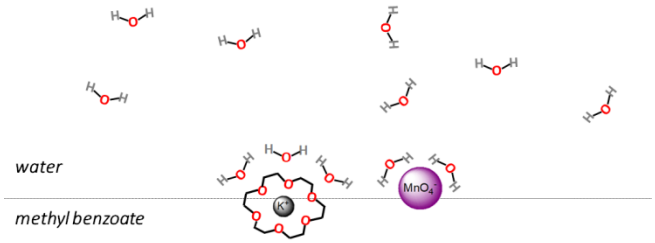

Figure 12b. Phase transfer of the salt, ions are partly hydrated, potassium ion is partly bound to a 18C6 molecule

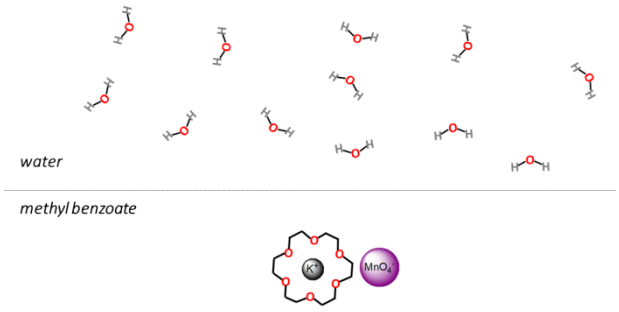

Figure 12c. Complete phase transfer, ions are completely dissolved in the methyl benzoate phase

Certain simplifications were made in the visualization. For example, only the solvation shell of the cation is shown, while the solvation of the 18C6 molecule in the organic medium is omitted. Likewise, the distribution of 18C6 between the aqueous and the methyl benzoate phase is not depicted. Furthermore, the cation and anion form a so-called ion pair in the organic phase in which the anion is bound above or below the molecular plane of the cation complex [1,37]. In the two-dimensional representation in Figure 12c, the anion is instead shown directly right

beside the cationic complex to indicate ion pairing. A more detailed discussion can be found in the supporting information.

For the 18C6-mediated $KMnO_4$ transfer, equation (4) applies:

$$K^+_{(aq)} + MnO^-_{4(aq)} + 18C6_{(o)} \rightleftharpoons K(18C6)MnO_{4(o)} \quad (4)$$

The (power point) animation showing complex formation, from which Figures 12a-c were taken, can be downloaded free of charge from the website cited in [38].

2.2.2. Decomplexation

Once the ionophore has transported a metal cation across the cell membrane, decomplexation occurs at the opposite side, releasing the cation into the aqueous cell interior (or exterior) (cf. section 1.2) [30,39]. To mimic this process, 2 mL of the $KMnO_4$/18C6 solution in methyl benzoate from the above complexation experiment is taken up with a syringe and then added to 1.5 mL of an aqueous 1 M magnesium sulfate ($MgSO_4$) solution. Following the example of PRESSMANN (cf. section 2.2.1), $MgSO_4$ is used to increase the density of the aqueous phase (ϱ(1 M $MgSO_4$) = 1.12 gmL^{-1}) so that it can be layered with the methyl benzoate solution of the 18C6/$KMnO_4$ mixture. As soon as the two phases are in touch, the bottom aqueous phase becomes colored due to the transfer of $KMnO_4$ (see Figure 13). For comparison, the representation of this step during *biological membrane transport* (see Figure 4) is shown in Figure 13. Accordingly, the solution of $KMnO_4$ in methyl benzoate with the potassium ion complexed by 18C6 represents the ionophore complex partitioned in the lipophilic cell membrane. The decomplexation step then takes place at the aqueous cell exterior (or interior).

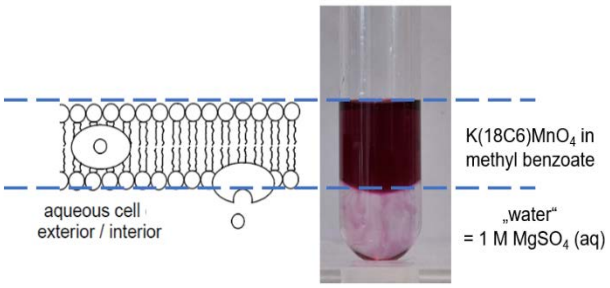

Figure 13. Comparison of the test tube experiment modelling decomplexation at the surface of the cell membrane

At the particle level, the process shown in Figure 12a-c is simply reversed, with the positions of the aqueous and organic phases interchanged. Since the metal cation is reversibly bound to the crown ether [11] and since the concentration of $KMnO_4$ is zero within the aqueous phase, the decomplexation process is initially very fast and becomes progressively slower until an equilibrium is reached [30]. During this process, water molecules solvate both components of the ion pair, thus mediating salt dissolution [11]. The reaction for the process is given by equation (5):

$$K(18C6)MnO_{4(o)} \rightleftharpoons K^+_{(aq)} + MnO^-_{4(aq)} + 18C6_{(o)} \quad (5)$$

An animation of the decomplexation process can be downloaded free of charge from the website given in [38].

2.2.3. Complexation-decomplexation (in a vertical PRESSMAN cell)

The two previous experiments are intended to prepare for the one, in which complexation and decomplexation are combined in *one* simple test tube experiment. This allows demonstrating the ionophore-facilitated transport of ions from the aqueous cell interior to the cell exterior (or vice versa) in its entirety in a single experiment.

For the experiment, 1.5 mL of a 1 M aqueous solution of $MgSO_4$ is placed in a test tube clamped in a stand, followed by adding a small stirring rod. This solution is layered with 2.5 mL of methyl benzoate and the methyl benzoate phase is then layered with 1.5 mL of a 0.1 M aqueous solution of $KMnO_4$ to obtain a triphasic system. No phase transfer of $KMnO_4$ into the organic phase is observed in the absence of a crown ether (Figure 14, left). Once 0.5 mL of a solution of 18C6 in methyl benzoate (c = 0.3 M) are added into the methyl benzoate phase with a help of a syringe, $KMnO_4$ is observed to pass first into the methyl benzoate phase (Figure 14, middle) and subsequently into the aqueous $MgSO_4$ solution (Figure 10, right). Meanwhile, the $MgSO_4$ solution is kept in motion by stirring in order to accelerate the phase transfer into the bottom phase. In order to minimize the time of the experiment, it can be helpful to stir the methyl benzoate phase with the needle of the syringe after the injection of the 18C6 solution. It is also possible to *carefully* sway the test tube back and forth a little to accelerate the phase transfer of the $KMnO_4$ from the methyl benzoate phase to the aqueous phase. The phase transfer of $KMnO_4$ from the top aqueous solution to the bottom one usually takes less than 5 minutes with freshly prepared solutions.

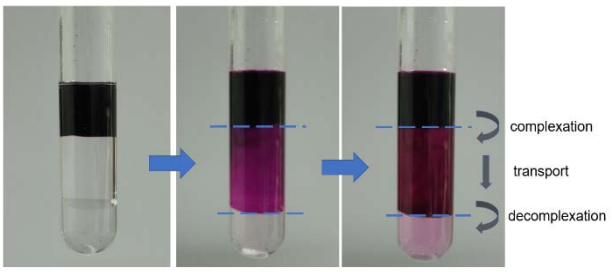

Figure 14. Complexation and decomplexation combined: Modelling the ionophore-facilitated transfer of potassium ions from the cell exterior (interior) into the cell interior (exterior) with the help of 18C6 and methyl benzoate in a triphasic system

Figure 15 provides a complete schematic comparison between the test tube experiment and ionophore-facilitated cation transport across a cell membrane.

In the model experiment, the upper aqueous phase represents the aqueous cell exterior (or interior), methyl benzoate represents the cell membrane and the $MgSO_4$ solution the aqueous cell interior (or exterior). The reactions given in equations (4) and (5) occur simultaneously at the phase boundaries. Again, the process is represented at particle level using the simplifications made in section 2.2.1. The animation of the combined complexation-decomplexation processes in

the test tube experiment can be downloaded free of charge at the link given in [38].

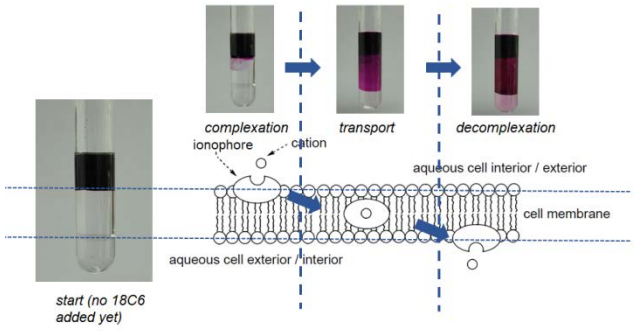

Figure 15. Comparison of the test tube experiment with the ionophore-facilitated cation transport across the cell membrane

3. Conclusion

The crown ether 18C6 mimics the structure and properties of valinomycin in that both molecules feature a cyclic arrangement of oxygen atoms around a cavity, allowing them to bind potassium ions in their hydrophilic interior so that a fat-soluble complex is obtained. In the case of valinomycin, the masked ions can penetrate the lipid membranes of cells and allow the cations to be transported from the outside into the cell interior or into the opposite direction. This disrupts the delicate potassium balance of the cells and initiates cell death, which explains the antibacterial properties of valinomycin (see section 1.2. and introduction of section 2)

A vertical PRESSMAN cell was developed using a simple test tube experiment to mimic this membrane transport process. In this experiment, methyl benzoate acts as the model membrane, separating an aqueous $MgSO_4$ and an aqueous $KMnO_4$ phase. When the liquid membrane contains 18C6 as the model ionophore, potassium ions are transported from the top $KMnO_4$ phase through the liquid membrane into the $MgSO_4$ solution. This process is visible to the naked eye by the concomitant transport of the intensively coloured permanganate ions, which follow the potassium ions to ensure charge compensation. For teaching purposes, the individual steps of this process, namely complexation, transport, and decomplexation, are illustrated using “step by step experiments” and simplified particle-level visualizations.

Other experiments using crown ethers to demonstrate supramolecular principles are currently under development. Importantly, parallels to fundamental biological processes are emphasized in all these experiments to extract overarching principles and develop a general understanding among students. The fact that biological contexts have been shown to motivate learners of all age groups (elementary [40], high school [41,42] and university/college students [43]) to engage with chemistry is particularly worth mentioning here.

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References

[1] F. Vögtle, E. Weber, *Host Guest Complex Chemistry / Macrocycles*. Berlin, Heidelberg: Springer Berlin Heidelberg, 1985.

[2] C. J. Pedersen, „The Discovery of Crown Ethers (Noble Lecture)“, *Angew. Chem. Int. Ed. Engl.*, 27(8), 1021–1027, Aug. 1988.

[3] J. F. Stoddart, „Introduction to Macrocycle Chemistry“, in *Crown Ethers and Cryptands*, The Royal Society of Chemistry, 1991, 1–21.

[4] C. J. Pedersen, H. K. Frensdorff, „Macrocyclic Polyethers and Their Complexes“, *Angew. Chem. Int. Ed. Engl.*, 11(1), 16–25, Jan. 1972.

[5] L. Fabbrizzi, „The origins of the coordination chemistry of alkali metal ions“, *ChemTexts*, 6 (2), Jun. 2020.

[6] F. Vögtle, „Wirt/Gast-Chemie mit Kationen und Anionen“, in *Supramolekulare Chemie*, in Teubner Studienbücher Chemie, Wiesbaden: Vieweg+Teubner Verlag, 1992, 23–167.

[7] S. Kubik, *Supramolecular Chemistry: From Concepts to Applications*; 2. Ed., De Gruyter: Berlin, 2024.

[8] P. Meyer, A. Banerji, "Macrocycles in the Classroom. Making Biochemical Processes Understandable with the Help of Crown Ethers"*14th “New Perspectives in Science Education - International Conference”*, New Perspectives in Science Education. IT: Filodiritto Editore - Pixel Associazione, Mar. 2025.

[9] https://www.nobelprize.org/prizes/chemistry/1987/summary/ [accessed, Jan. 20th 2026].

[10] J. Lehn, „Supramolecular Chemistry—Scope and Perspectives Molecules, Supermolecules, and Molecular Devices (Nobel Lecture)“, *Angew. Chem. Int. Ed. Engl.*, 27(1), 89–112, Jan. 1988.

[11] J. W. Steed, D. R. Turner, K. J. Wallace, *Core concepts in supramolecular chemistry and nanochemistry*. Chichester: J. Wiley & sons, 2007.

[12] S. Huang, Y. Liu, W.-Q. Liu, P. Neubauer, und J. Li, „The Nonribosomal Peptide Valinomycin: From Discovery to Bioactivity and Biosynthesis“, *Microorganisms*, 9 (4), 780, Apr. 2021.

[13] H. Brockmann, G. Schmidt-Kastner, „Valinomycin I, XXVII. Mitteil. über Antibiotica aus Actinomyceten“, *Chem. Ber.*, 88 (1), 57–61, Jan. 1955.

[14] B. C. Pressman, E. J. Harris, W. S. Jagger, J. H. Johnson, „Antibiotic-mediated transport of alkali ions across lipid barriers.“, *Proc. Natl. Acad. Sci. U.S.A.*, 58 (5), 1949–1956, Nov. 1967.

[15] M. Sulik, R. Graniczny, J. Janczak, D. Kłopotowska, J. Wietrzyk, A. Huczyński, „From Pseudocyclic to Macrocyclic Ionophores: Strategies toward the Synthesis of Cyclic Monensin Derivatives“, *J. Org. Chem.*, 90 (3), 1344–1353, Jan. 2025.

[16] M. Antoszczak, „A comprehensive review of salinomycin derivatives as potent anticancer and anti-CSCs agents“, *European Journal of Medicinal Chemistry*, 166, 48–64, March 2019.

[17] W. Monden, G. Kosmann, H. Harder, „Zur Permeation von Ionen durch Biomembranen“, *Unterricht Biologie*, 46 (4), 40–43, 1980.

[18] P. Y. Bruice, *Organische Chemie: Studieren kompakt*, 5., Aktualisierte Auflage. in Always learning. München: Pearson Studium, 2011.

[19] C. J. Pedersen, „SYNTHETIC MULTIDENTATE MACROCYCLIC COMPOUNDS“, in *Synthetic Multidentate Macrocyclic Compounds*, Elsevier, 1978, 1–51.

[20] L. Sessa, S. Concilio, F. Marrafino, A. Sarkar, R. Diana, S. Piotto, „Theoretical investigation of hydroxylated analogues of valinomycin as potassium transporter“, *Computational Biology and Chemistry*, 106, 107936, Oct. 2023.

[21] F. Ullah, T.A. Khan, J. Iltaf; S. Anwar, M.F.A. Khan, M.R. Khan, S. Ullah, M. Fayyaz ur Rehman, M. Mustaqeem, K. Kotwica-Mojzych et. al. „Heterocyclic Crown Ethers with Potential Biological and Pharmacological Properties: From Synthesis to Applications“, *Applied Sciences*, 12 (3), 1102, Jan. 2022.

[22] J. D. Lamb, J. J. Christensen, R. M. Izatt, „Experimenting with liquid membranes“, *J. Chem. Educ.*, 57(3), 227, Mar. 1980.

[23] D. H. Haynes und B. C. Pressman, „Two-phase partition studies of alkali cation complexation by ionophores“, *J. Membrain Biol.*, 18 (1), 1–21, Dec. 1974.

[24] B. C. Pressman, „Ionophorous antibiotics as models for biological transport“, *Fed Proc*, 27 (6), 1283–1288, 1968.

[25] R. Ashton, L. K. Steinrauf, „Thermodynamic consideration of the ion transporting antibiotics“, *Journal of Molecular Biology*, 49 (3), 547–556, May 1970.

[26] G. W. Gokel, S. Negin, M.R. Cantwell, „Crown Ethers“, in *Comprehensive Supramolecular Chemistry II*, Elsevier, 2017, 3–48.

[27] R. D. Dyson, *Cell biology: a molecular approach*, 2. ed. Boston: Allyn and Bacon, 1978.

[28] B. C. Pressman, N. T. De Guzman, „NEW IONOPHORES FOR OLD ORGANELLES*“, *Annals of the New York Academy of Sciences*, 227 (1), 380–391, Feb. 1974.

[29] M. Kirch, J. Lehn, „Selective Transport of Alkali Metal Cations through a Liquid Membrane by Macrobicyclic Carriers“, *Angew. Chem. Int. Ed. Engl.*, 14 (8), 555–556, Aug. 1975.

[30] C. F. Reusch, E. L. Cussler, „Selective membrane transport“, *AIChE Journal*, 19 (4), 736–741, Jul. 1973.

[31] „Valinomycin, Sigma Aldrich“.

[32] J. Friedrich; M. Oetken, „Modellexperimente zum Durchtritt von Ionen durch eine Biomembran“, *Praxis der Naturwissenschaften - Chemie in der Schule*, 62 (8), 29–34, 2013.

[33] P. Meyer, A. Banerji, „Wie Kationen Zellwände durchdringen“, *Nachr Chem*, 72 (7–8), 28–32, Jul. 2024.

[34] Md. M. Mostafiz, E. Hassan, K.-Y. Lee, „Methyl Benzoate as a Promising, Environmentally Safe Insecticide: Current Status and Future Perspectives“, *Agriculture*, 12 (3), 378, Mar. 2022.

[35] H. J. Bader, H. Schmidtkunz, „Das Experiment im Chemieunterricht“, in *Konkrete Fachdidaktik Chemie*, Neubearb., 3. ed., P. Pfeifer, B. Lutz, und H. J. Bader, Hrsg., München: Oldenbourg, 2002.

[36] A. Banerji, A. Schönbein, J. Wolff, „OLED Reloaded: Die Synthese des Halbleiterpolymers MEH-PPV als Schulversuch“, *Chemkon*, 24 (4), 251–256, 2017.

[37] D. J. Sam, H. E. Simmons, „Crown polyether chemistry. Potassium permanganate oxidations in benzene“, *J. Am. Chem. Soc.*, 94 (11), 4024–4025, May 1972.

[38] https://banerji-lab.com/downloads/ [accessed, Jan. 20th 2026].

[39] G. Gokel, A. Nakano, „Feeble Forces and Flexible Frameworks“, in *Crown Compounds. Toward Future Applications*, Weinheim: VCH, 1992, 1–26.

[40] M. K. Janssen, „Mit biologischen Inhalten Brücken zur Chemie bauen. Entwicklung und Erprobung eines Seminars für Sachunterrichtsstudierende“, Universität Siegen, Siegen.

[41] J. Lewing, P. Klein, S. Schneider, „Wirkung technischer und biologischer Kontexte auf das situationale Interesse beim Bearbeiten physikalischer Lernaufgaben zum Energiekonzept“, *ZfDN*, 29 (1), 8, Dec. 2023.

[42] J. Bennett, F. Lubben, „Context-based Chemistry: The Salters approach“, *International Journal of Science Education*, 28 (9), 999–1015, Jul. 2006.

[43] L. Mendez, A. T. Rivera, I. Vasquez, A. Godínez Aguilar, M. T. Owens, und C. L. Meaders, „How students taking introductory biology experience the chemistry content“, *J Microbiol Biol Educ.*, 25(3), e00111-24, Dec. 2024.