CYCLODEXTRIN NEWS

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Computational simulations of cyclodextrins: are you ready?

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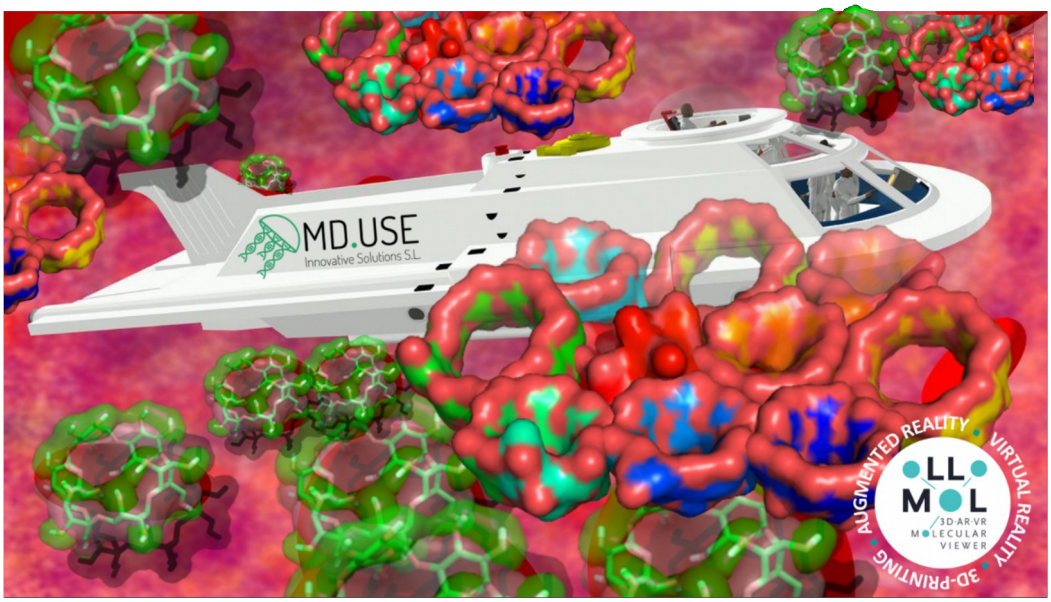
Abstract

Computational simulations are nowadays ubiquitous. They are employed to predict the behavior of populations under certain conditions, to design cars, buildings and other large structures such as bridges or roads, and also to develop new drugs. The work in these areas is inconceivable nowadays without computational simulations. In particular, Molecular Dynamics (MD) simulations are highly powerful to study the behavior and features of molecular systems since they allow determining a large number of energetic, structural and dynamic properties and also elucidating interaction mechanisms as well as the evolution of complex structures as a function of time with atomic resolution. The contribution of MD simulations to the study of molecular systems has been recognized with the Nobel Prize in Chemistry in 2013, awarded to three of the main developers of the technique (Martin Karplus, Michael Levitt and Arieh Warshel). Surprisingly, computational simulations are not commonly employed for the study of cyclodextrins (CDs) even though these molecules, due to their relatively small size, are well suited for this kind of methodologies. Here, we show evidences about the important contribution that MD simulations might have on the study of CD systems including the characterization of inclusion and non-inclusion complexes, the formation of aggregates and the adsorption to polar/nonpolar interfaces. Since these computational simulation studies are based on the coordinates of all atoms in the three-dimensional space, we implemented for the first time the use of Augmented Reality (AR) and Virtual Reality (VR) technologies to visualize the results. This allows viewing CDs in a previously inconceivable way, not only in three dimensions and from any angle or position in the space but also in movement. We provide AR patterns together with free access to applications for smartphones to illustrate how this works.



Cyclodextrins are not simple rigid truncated cones

Humans tend to simplify the real world by using rude representations of complex objects. Cyclodextrins (CDs) are not simple at structural, dynamic and functional levels but for many years the native α-, β- and γ-CDs have been represented by perfect truncate cones of different diameters.

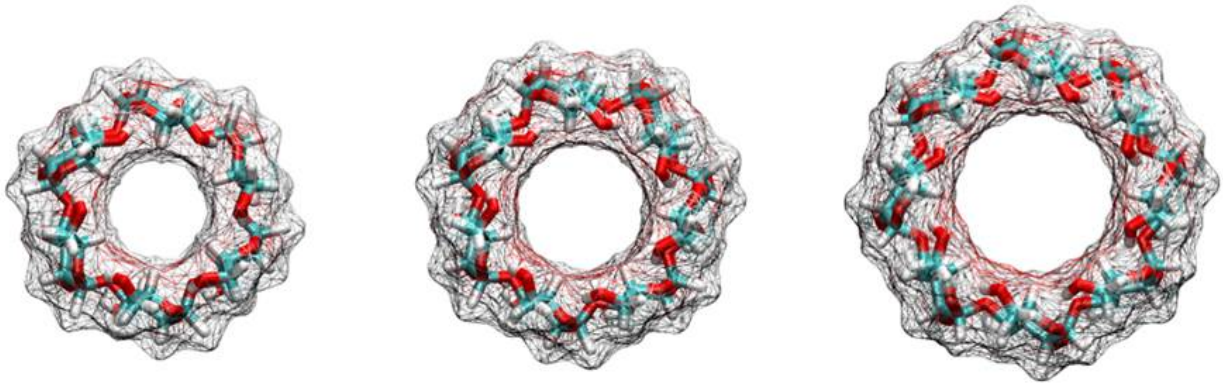


Figure 1: Typical representation structure of native α-, β- and γ-CDs as rigid truncated cones.

Such a simple representation does not explain some physicochemical properties of these molecules including their different solubility as well as their ability to encapsulate a large variety of molecules with different stoichiometry and probability (affinity). It is easy to understand that two amphiphilic molecules with identical polar groups and aliphatic chains of different length as nonpolar groups have different solubility or ability to self-aggregate. In this case the weight of the hydrophobic region justifies the differences. The same reasoning cannot be applied to explain the fact that the solubility of the native β-CD is about one order of magnitude lower than that of α-CD and γ-CD [Mixcoha et al., 2014] because their structures cannot be clearly divided in polar/nonpolar regions -the identification of the cavity as a nonpolar region is an oversimplification. Similarly, CDs can solubilize molecules which do not fit into their cavities throughout different mechanisms: non-inclusion complexes or by aggregating around them like a micelle [Messner et al., 2010]. The energy of solvation for the monomeric species competes with the energy of self-aggregation and CD aggregates can play an important role in many processes [Mixcoha et al., 2014]. Additionally, it has been proven

that CDs are highly flexible [Dodziuk, 2002] and this is difficult to conciliate with the simplistic truncated cone view of these molecules. Everything becomes more complex for non-native CDs where the hydrogen atoms of some primary or/and secondary hydroxyl groups are replaced by other chemical groups. Modified CDs are usually represented as truncated cones with disordered branches. Again, this representation is simple but not fair with the real complexity of the structures. The number of degrees of freedom dramatically increases in these cases.

Another factor that contributes to increase the complexity in the study of modified CDs is that they are typically supplied as heterogeneous distributions of structures with the substitutions located at the different hydroxyl groups with different probability. This means that the distribution of substitutions not only changes in number but also in the specific locations, depending on the synthesis route. On top to the behavior of these molecules at equilibrium as single solutes -or in the presence of co-solutes- as a function of their concentration, it is important to consider the dynamics as well as the kinetics of the different processes. Some events like the self-aggregation or dissociation in the presence of different co-solutes take place at the time scale of hours or even days [Gaitano et al., 1997] while others like the conformational change of an inclusion complex are very quick and they can only be seen at the time scale of picoseconds (ps) or nanoseconds (ns) [Piñeiro et al., 2007].

The behavior of CDs and CD complexes at polar/nonpolar interfaces is also extremely interesting. The group of Eric Monflier at the University of Artois has performed a lot of experimental work on this issue. They found that different substitutions on the native CDs have a large impact on their interfacial properties [Leclercq, 2007]. They have also connected these results with the ability of CD aggregates to encapsulate different molecules as well as to use such superstructures as green chemical reactors [Ferreira et al., 2012]. Interfacial films with interesting mechanical properties based on α-CD complexes with sodium dodecyl sulfate have also been recently observed [Hernández-Pascacio et al., 2007] and the exotic self-assembly behavior of the same structures in solution at high concentration has been studied by different experimental techniques [Jiang et al., 2011]. More complex structures such as cyclodextrinosomes, also formed at polar/nonpolar environments, have been reported by Mathapa and Paunov, who proposed several practical applications for these systems [Mathapa and Paunov, 2013].

Purely experimental information is rarely useful

Clearly, the rigid truncated cone view of CDs is useful for simple representations but not to explain the formation of the previously described structures either the properties of these molecules and the derived molecular assemblies. A large number of experimental methods based on different measurement principles (calorimetry, different spectrometric and microscopy methods, several methods based on nuclear magnetic resonance, surface tension, X-ray and neutron reflectometry/scattering, etc.) have been applied to extract information on CD-based systems. Each of these methods is typically focused on a particular aspect: energy, structure at different level or in different locations, kinetics, etc. In general, the useful results at quantitative level are not purely experimental but they are connected to a primary signal throughout a model with assumptions that are more or less accurate. Additionally, the application of a given model requires a pre-processing of the raw measurements that is often accompanied by a loss of information. In many cases, completely different models with divergent conclusions are able to describe reasonably well a given set of experimental data. Purely experimental results providing useful specific and quantitative information for molecular systems -with no modelling steps- are hard to imagine.

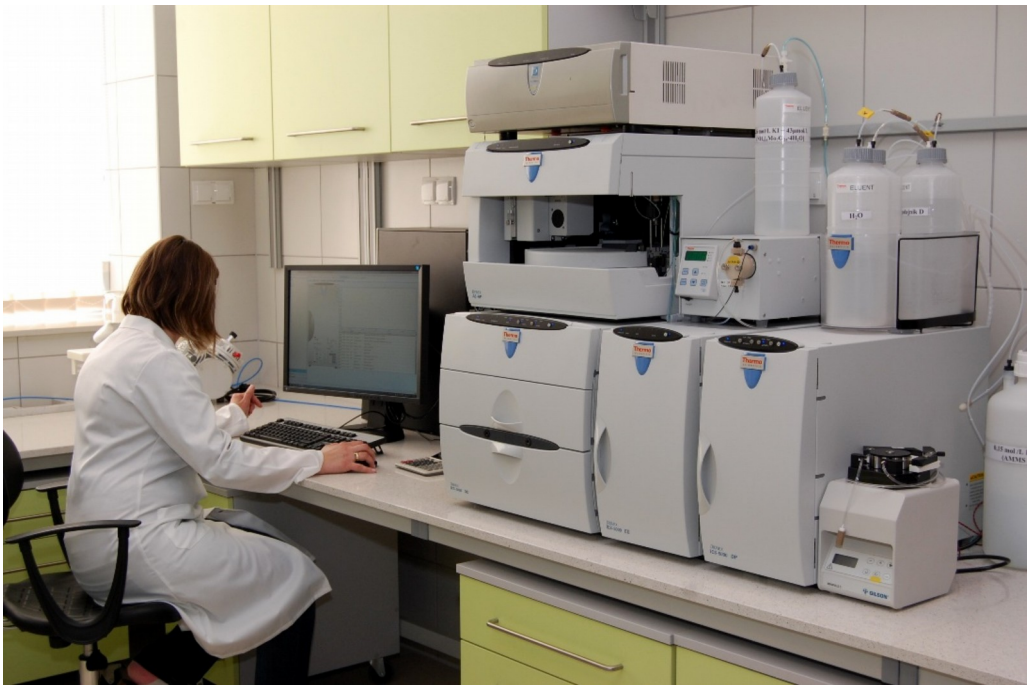


Figure 2: Example of wet-lab experiments**.** Almost all experiments are coupled to modelling steps to treat the measured signals, so "pure" experimental information is commonly not useful.

The power of Computational Simulations

Nowadays, weather forecasting is unthinkable without computational simulations based on information collected by strategically distributed sensors and satellites. The design of expensive structures such as buildings or bridges, functional instruments, technological devices, etc. are also based on computational simulations. The development of new active principles in the pharmaceutical industry also makes intensive use of computational simulations at different levels.

The rapid evolution of hardware and new algorithms makes increasingly trustworthy the results of computational work because it facilitates the sampling of the involved structures and so the calculation of new properties and the elucidation of mechanisms for specific processes.

Surprisingly, computational simulations of CD systems are scarce even though they are relatively small molecules compared with typical proteins and other biological structures. Thus, CDs are easily accessible to computational methods, but several difficulties prevent their use for these systems: the lack of computational tools specifically developed for them as well as of well-validated force field and simulation parameters. In the case of protein systems both issues have been overcome several years ago due to the high demand of tools for those systems, but CDs are much more specific molecules and much less effort has been put on them.

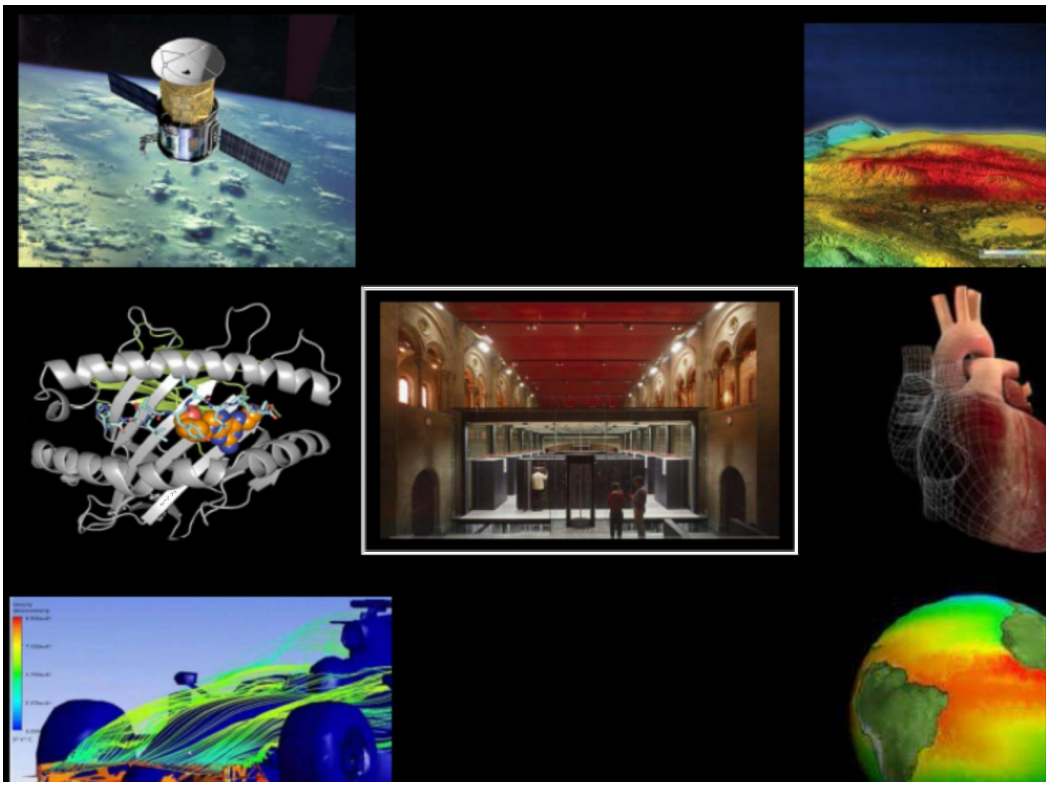


Figure 3: Examples of the use of computational simulations in different areas, i. e. weather prediction, medicine, car industry, pharmacy, aerospace industry, etc. Supercomputers are used in all of them.

Molecular Dynamics simulations of Cyclodextrins

MDUSE Innovations has internally developed and validated specific tools to perform Molecular Dynamics (MD) simulations of native and modified CDs. Our scientific team has participated in both experimental and theoretical studies of CD systems including the formation of inclusion and non-inclusion complexes of different stoichiometry, the aggregation of native CDs and CD complexes, the adsorption to polar/nonpolar interfaces and the formation of CD based films [Hernández-Pascacio et al., 2007].

Experiments and computational simulations together, when they converge to compatible results, provide a quite complete view of the studied systems. By comparing the results obtained from different force fields and simulation parameters for CDs we have seen that they are especially sensitive to all these parameters. Thus, we have developed a specific parameterization of the GROMOS force field for CDs that, in contrast to other combinations of parameters, provides results perfectly compatible with a variety of experiments both in solution and at interfaces (Mixcoha et al., 2014; Brocos et al., 2010; Piñeiro et al., 2007) (see Figure 4). A feature of this parameterization is that the simulated CDs are significantly more flexible than CDs simulated using other force fields. This allows seeing more events during a MD trajectory as well as catching the most stable structures.

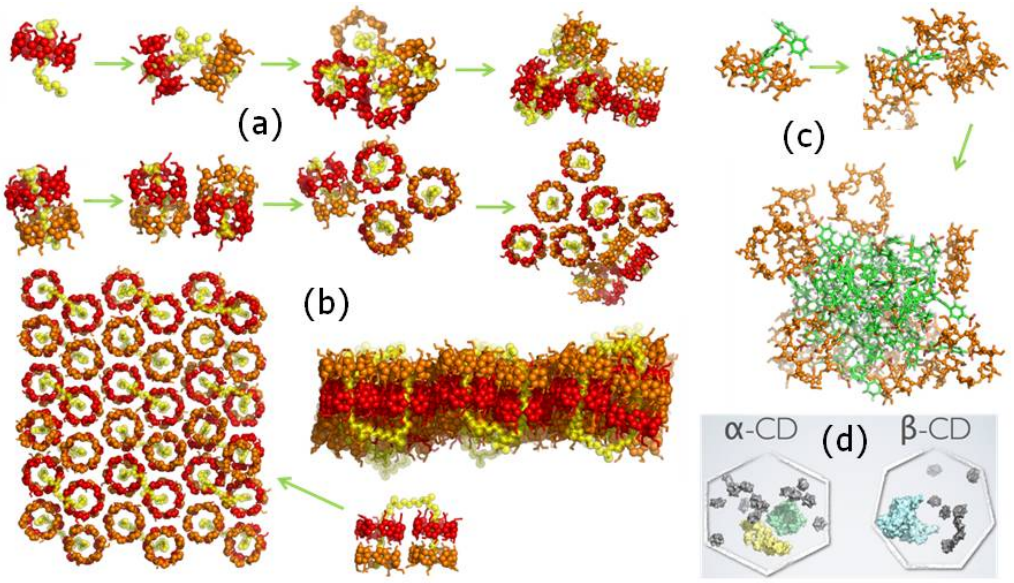


Figure 4: Different examples of simulation studies of CD systems forming inclusion complexes of different stoichiometry with surfactant molecules, aggregation between different number of 1:1 and 2:1 complexes (a), self-assembly of 4:1 complexes of α-CD with a gemini surfactant forming a bilayer (b), aggregates of relatively small phosphane molecules surrounded by native β-CDs (c) and self-aggregates of pure native α- and β-CDs (d).

The negative side of simulation democracy

As discussed above, well-designed MD simulations of CD systems are highly powerful. During the last years, a number of tools designed to facilitate the simulation of molecules have been developed and nowadays it is relatively easy to see how a molecule moves by using automated and user friendly commercial software. This democratization of the technique is positive when the users know how to manage the tools. However, such facilities have favored the publication of computational simulations of molecules that are not properly designed and analyzed. MD simulations, like any experimental property, should not be employed to get results beyond the limitations of the technique and the obtained trajectories should not be overanalyzed. In order to perform a computational simulation, a good knowledge of the system from the experimental point of view and also on the simulation methods specifically adapted for the target molecules is recommended. General methods developed mainly for proteins or other specific kind of molecules should not be directly extrapolated to CDs. Validation of force fields and simulation parameters is always recommended.

Doing analysis of Molecular Dynamics simulation trajectories

MD simulations, as well as the analysis of the resulting trajectories, are designed for specific aims. Typically, they are devoted to the elucidation of interaction mechanisms or to the determination of some quantitative property such as global or specific distances or angles, energy contributions or movement periods. The amount of information contained in the MD trajectories is huge since all the atomic coordinates are stored every few picoseconds. As an example, we have recently determined the solvation free energies of native CD monomers at different temperatures (Mixcoha et al., 2014), concluding that the role of CD aggregation in the solubility of these molecules is key to understand this property. Binding free energies for host-guest complexes have been computed by several authors (Henriksen and Gilson, 2017).

A very important part of the analysis is the visualization. For this it is important to note that CD complexes are not flat but highly involved in the three spatial dimensions and they usually move in non-trivial ways.

AR/VR visualization

Augmented Reality and Virtual Reality technologies are nowadays easily accessible from medium-high range smartphones with more than reasonable quality. The extraordinarily quick advance that these methods are experiencing encourages us to expand the variety of applications in different fields. In particular, the dynamic features of CD-based structures and other complex molecular systems can be efficiently represented thanks to Augmented Reality (AR) and Virtual Reality (VR) devices and software. Since molecular systems are naturally three dimensional, the level of immersion provided by AR/VR to visualize their movement in 3D and at 360º favors a much better understanding of the interactions that define their behavior.

3D printing technology is also advancing very quickly, and it is getting easier to create 3D-printable models of molecules that are scientifically correct.

The combination of these visualization methods with computational simulation techniques allows reaching an explicit understanding of the systems under study that otherwise can only be imagined. The growth of AR, VR and 3D-printing to enhance illustrations of chemical and biological communications at papers (Muslo et al., 2016), meetings, conferences, and trade shows in recent years means these technologies appear here to stay and to greatly expand how publishers, writers, event hosts, exhibitors, and sponsors interact with their audience. Our company has recently developed the software Ollomol (available at the ios and android official stores for free) that implements this technology to visualize molecular systems and, in particular CD complexes. Some illustrations of this software are shown in Figure 5.

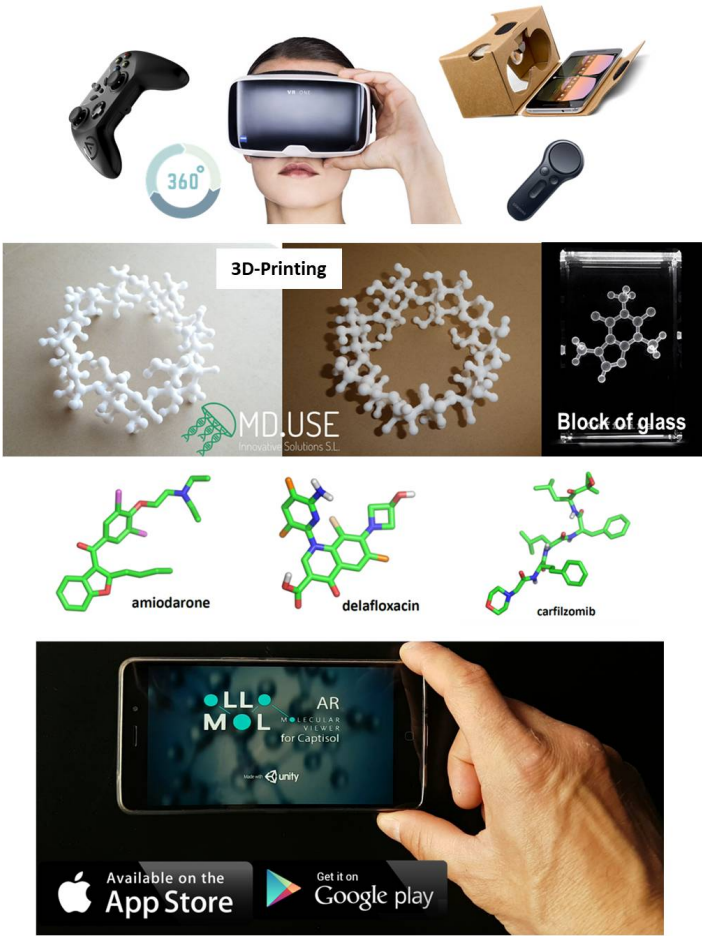


Figure 5: Virtual Reality, Augmented Reality and 3D-printing applied to CD systems. *Visit the Oculus app repository and look for "**Ollomol VR"** to download our app for **VR** for free using the Samsung Gear headset. Visit the app store for ios or the play store for android and download the "**Ollomol AR"** molecular viewer for free if you want to test our **AR** technology.* Just point to the green molecules in this figure and you will see the magic yourself!

Conclusions

The final conclusions obtained from experimental work in molecular systems depend a lot on the following factors: the purity and homogeneity of the samples, the sensitivity of the instrument and the principle of measurement to be applied, the processing of the raw data, the application of a reasonable model and the fitting of the parameters with physical meaning avoiding local minima and over-parameterization as well as getting a good estimation of uncertainties. A fail in any of these steps makes an experiment completely useless. Most of these factors are perfectly under control in computational simulations. Of course, different uncertainties, such as the size of the sample that is possible to simulate during a reasonable time and the quality of the employed force field, appear in this case. A well-designed simulation can provide information that is extremely difficult to obtain in a wet lab and modern visualization methods such as AR and VR are highly efficient to show the structural and dynamic behavior of these molecules in a very clear way. We do encourage you, the reader, to test these new technologies to study your molecular systems by contacting us (info@mduse.com).

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Hernández-Pascacio, J., Garza, C., Banquy, X., Díaz-Vergara, N., Amigo, A., Ramos, S., Castillo, R., Costas, M. and Piñeiro, Á. Cyclodextrin-based self-assembled nanotubes at the water/air interface. *J. Phys. Chem. B* **2007**, 111 (44), 12625.

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Messner, M., Kurkov, S.V., Jansook, P. and Loftsson, T. Self-assembled cyclodextrin aggregates and nanoparticles. *Int. J. Pharmaceutics*. **2010**, 387, (1–2), 199.

Mixcoha, E., Campos-Terán, J. and Piñeiro, Á. Surface adsorption and bulk aggregation of cyclodextrins by computational molecular dynamics simulations as a function of temperature: α-CD vs β-CD. *J. Phys. Chem. B*, **2014**, 118 (25), 6999.

Musio, B., Mariani, F., Śliwińskia, E.P., Kabeshova, M.A., Odajimac, H. and Ley, S.V. Combination of enabling technologies to improve and describe the stereoselectivity of Wolff–Staudinger cascade reaction. *Synthesis* **2016**, 48(20), 3515.

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Cyclodextrin News Retrospective

We wrote 10, 20 and 30 years ago

10 years ago, the editorial of Cyclodextrin News dealt with the use of cyclodextrins for controlling the ripening of fruits. Hard picked fruits better survive transport, but need to undergo „programmed ripening" before offered for sale at stores. 1-methylcyclopropene gas used for delaying ripening was introduced in molecularly encapsulated form attained by α-cyclodextrin and could be distributed as a powder (called SmartFresh). Now, in 2017, according to the current homepage of the manufacturing company (https://www.agrofresh.com/smartfresh-technology) the product is still successful, moreover available in three additional modes of delivery: ProTabs (tablet), SmartTabs (for small quantities) or InBox (sachet format to be used in container).

K. Balogh: „Cyclodextrin for control the ripening of fruits" Cyclodextrin News, 2007 Vol. 21, No. 11.

20 years ago, Cyclodextrin News editorial reported on the EU project entitled „Development from CD derivatives to polymeric materials for selective transport, separation and detection of active substances." The program coordinator was Professor Wenz, while the participating groups were led by outstanding researchers as M. Morcellet, G. Torri, B. Perly, J. Defaye, D. Reinhoudt, W.A. König, J.M. Bardin, P. Kilz, J. Vessman and G. Schmid. The aim of the EU project was to find new applications for functional CD derivatives and CD polymers.

J. Szejtli: „EU Project Report on utilisation of CD", Cyclodextrin News, 1997 Vol. 11, No. 11.

30 years ago, in the second volume of Cyclodextrin News, the topic highlighted by Professor Szejtli was the deodorant effect of CDs. A simple calculation method showed that using cyclodextrin even in the case of lower association constant (K_a) values, significant smell reduction may be expected. Several examples such as hair-wave setting compositions, mouth deodorant, palatable soybean, yeast, vitamin B_1 products were enumerated. The viability of the concept is best demonstrated by the over 20-year success of a flagship product of Procter & Gamble: Fabreeze / Febreze which was introduced in 1996.

J. Szejtli: „Deodorant effect of CDs" Cyclodextrin News, 1987 Vol. 2, No. 3.

Bibliography & Keywords of Selected Publications of the Month

Qiu, C.; Wang, J.; Fan, H.; Bai, Y.; Tian, Y.; Xu, X.; Jin, Z.

High-efficiency production of γ-cyclodextrin using β-cyclodextrin as the donor raw material by cyclodextrin opening reactions using recombinant cyclodextrin glycosyltransferase

βCD as raw material for the production of γCD, Ring opening reaction in the presence of maltose

Carbohydrate Polymers, 2018, 182, 75-80

Ye, Y.; Ren, H.; Zhu, S.; Tan, H.; Li, X.; Li, D.; Mu, C.

Synthesis of oxidized β-cyclodextrin with high aqueous solubility and broad-spectrum antimicrobial activity

Hydrogen peroxide, Carbonyl and carboxyl functions, Aspergillus niger

Carbohydrate Polymers, 2017, 177, 97-104

Hashidzume, A.; Kuse, A.; Oshikiri, T.; Adachi, S.; Yamaguchi, H.; Harada, A.

A pseudo-rotaxane of β-cyclodextrin and a two-station axis molecule consisting of pyridinium and decamethylene moieties, and its deuteration in deuterium oxide

Shuttle, CD-catalyzed deuteration

Tetrahedron, 2017, -

Huang, H.; Juan, A.; Katsonis, N.; Huskens, J.

Competitive inclusion of molecular photo-switches in host cavities

βCD, Cucurbit[8]uril (CB[8]), Light-driven host exchange

Tetrahedron, 2017, -

Wang, H.; Sun, D.; Liao, H.; Wang, Y.; Zhao, S.; Zhang, Y.; Lv, G.; Ma, X.; Liu, Y.; Sun, G.

Synthesis and characterization of a bimodal nanoparticle based on the host-guest self-assembly for targeted cellular imaging

Bimodal MRI and NIR self-assembled supramolecular nanoparticle, Self-assembly of host-guest interactions between hyaluronic acid–βCD and amantadine-modified imaging agents

Talanta, 2017, 171, 8–15

Otremba, T.; Ravoo, B. J.

Dynamic multivalent interaction of phenylboronic acid functionalized dendrimers with vesicles

PAMAM dendrimers, Cyclodextrin vesicles decorated with a catechol-adamantane conjugate

Tetrahedron, 2017, -

Tao, J.; Xu, J.; Chen, F.; Xu, B.; Gao, J.; Hu, Y.

Folate acid-Cyclodextrin/Docetaxel induces apoptosis in KB cells via the intrinsic mitochondrial pathway and displays antitumor activity in vivo

Inducing mitochondrial-mediated apoptosis, Accumulation in tumor cells

European Journal of Pharmaceutical Sciences, 2018, 111, 540-548

Wu, M.; Liu, X.; Jin, W.; Li, Y.; Li, Y.; Hu, Q.; Chu, P. K.; Tang, G.; Ping, Y.

Targeting ETS1 with RNAi-based supramolecular nanoassemblies for multidrug-resistant breast cancer therapy

Adamantane-conjugated doxorubicin, Polyethyleneimine-modified HPβCD, Enhanced drug residence time at tumor site, Drug-resistant tumor-bearing mouse

Journal of Controlled Release, 2017, 253, 110-121

Adeoye, O.; Cabral-Marques, H.

Cyclodextrin Nanosystems in Oral Drug Delivery: A Mini Review

Bioavailability Biodistribution, Nanosystems, Nanoassemblies, Nanosponges, Nanofibers, Molecular imprints

International Journal of Pharmaceutics, 2017, -

Agnes, M.; Thanassoulas, A.; Stavropoulos, P.; Nounesis, G.; Miliotis, G.; Miriagou, V.; Athanasiou, E.; Benkovics, G.; Malanga, M.; Yannakopoulou, K.

Designed positively charged cyclodextrin hosts with enhanced binding of penicillins as carriers for the delivery of antibiotics: the case of oxacillin

Ampicillin, Amoxicillin, Methicillin, Oxacillin, Octakis(6-(2-aminoethylthio)-6-deoxy)-γCD, Cell crossing capability, Internalization into macrophages

International Journal of Pharmaceutics, 2017, -

Blatnik, J. A.; Thatiparti, T. R.; Krpata, D. M.; Zuckerman, S. T.; Rosen, M. J.; Von Recum, H. A.

Infection Prevention Using Affinity Polymer Coated, Synthetic Meshes in a Pig Hernia Model

MRSA, Cyclodextrin-based polymer crosslinked onto multifilament polyester mesh, Vancomycin, Clearing antibiotic resistant bacteria

Journal of Surgical Research, 2017, -

Elmowafy, M.; Samy, A.; Abdelaziz, A. E.; Shalaby, K.; Salama, A.; Raslan, M. A.; Abdelgawad, M. A.

Polymeric nanoparticles based topical gel of poorly soluble drug: Formulation, *ex vivo* and *in vivo* evaluation

Poly (ε-caprolactone), HPBCD polymers, Ex vivo human skin permeation and anti-inflammatory and analgesic activities, Topical delivery of indomethacin

Beni-Suef University Journal of Basic and Applied Sciences, 2017, -

Farooq, K.; Hunter, J. M.

Neuromuscular blocking agents and reversal agents

Review, Depolarizing and non-depolarizing agents, Nicotinic receptor. Depolarizing agents (e.g. suxamethonium) act as agonists like ACh at the nicotinic receptor, Sugammadex

Anaesthesia & Intensive Care Medicine, 2017, -

Loftsson, T.; Stefánsson, E.

Cyclodextrins and topical drug delivery to the anterior and posterior segments of the eye

Lipophilic drugs, Microparticles, Dorzolamide, Dexamethasone

International Journal of Pharmaceutics, 2017, -

Tian, Z.; Si, L.; Meng, K.; Zhou, X.; Zhang, Y.; Zhou, D.; Xiao, S.

Inhibition of influenza virus infection by multivalent pentacyclic triterpene-functionalized per-O-methylated cyclodextrin conjugates

1,3-Dipolar cycloaddition click reaction, Hemagglutination inhibition

European Journal of Medicinal Chemistry, 2017, 134, 133-139

Li, L.; Yu, L.; Hou, X.

Cholesterol-rich lipid rafts play a critical role in bovine parainfluenza virus type 3 (BPIV3) infection

Methyl-βCD, Lipid rafts in viral envelop, Lipid rafts in host cells

Research in Veterinary Science, 2017, -

Fernandes, A.; Rocha, M. A. A.; Santos, L. M. N. B. F.; (…); Mateus, N.; de Freitas, V.

Blackberry anthocyanins: β-Cyclodextrin fortification for thermal and gastrointestinal stabilization

Food colorants, βCD, Thermal stabilization, Stabilization under simulated gastrointestinal conditions

Food Chemistry, 2018. 245, 426-431

Pereira, A. B.; da Silva, A. M; Barroca, M. J.; Marques, M. P. M.; Braga, S. S.

Physicochemical properties, antioxidant action and practical application in fresh cheese of the solid inclusion compound γ-cyclodextrin·quercetin, in comparison with β-cyclodextrin·quercetin

Anti-peroxidation capacity, Nutraceutical additives in fresh cheese

Arabian Journal of Chemistry, 2017, -

Pragadheesh, V. S.; Chanotiya, C. S.; Rastogi, S.; Shasany, A. K.

Scent from Jasminum grandiflorum flowers: Investigation of the change in linalool enantiomers at various developmental stages using chemical and molecular methods

Fragrant garlands, Ethyl- and acetyl-βCD stationary phase.

Phytochemistry, 2017, 140, 83–94

Chang, F.; Zhou, Q.; Pan, H.; Liu, X.-F.; Zhang, H.; Yang, S.

Efficient production of biodiesel from Xanthium sibiricum Patr oil via supramolecular catalysis

Heterogeneous catalysts from cyclodextrins and Mg or Zn salts, Converting sustainable plant oils to biodiesel under mild conditions

Renewable Energy, 2017, -

Hu, Y.; Yan, C.; Chen, D.; Lv, C.; Jiao, Y.; Chen, G.

One-dimensional Co_3O_4 nanonet with enhanced rate performance for lithium ion batteries: Carbonyl-*β*-cyclodextrin inducing and kinetic analysis

Construction of nanonet, Crosslinking agent

Chemical Engineering Journal, 2017, 321, 31-39

Chang, D., Yan, W., Han, D., Wang, Q., Zou, L.

A photo-switchable dual-modality linear supramolecular polymer based on host−guest interaction of cyclodextrin and pseudorotaxane

Au nanoclusters loaded on nano-TiO2 surface, HS-βCD, Rhodamine B-labeled prion

Dyes and Pigments, 2018, 149, 188-192

He, L.; Gao, F.; Li, E.; Lee, J. T.; Bian, L.; Armstrong, D. W.

Chromatographic separation of racemic praziquantel and its residual determination in perch by LC-MS/MS

HPβCD superficially porous particle (SPP) column, Praziquantel enantiomers

Talanta, 2017, -

Li, X.; Li, J.; Liu, Y.; Zhang, X.; Chen, J.

A sensitive electrochemical immunosensor for prion detection based on poly-β-cyclodextrin/gold nanoparticles/glassy carbon electrode

βCD units to capture the prion antibody

Sensors and Actuators B: Chemical, 2017, 250, 1-7

Sedghi, R.; Heidari, B.; Yassari, M.

Novel molecularly imprinted polymer based on β-cyclodextrin@graphene oxide: Synthesis and application for selective diphenylamine determination

Molecularly imprinted polymer (MIP) for the determination of diphenylamine (DPA)

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