BIOVIA

3DEXPERIENCE®

IN SILICO THERAPEUTICS DELIVERY AND DEVELOPMENT WITH BIOVIA MATERIALS STUDIO

Datasheet

Effective drug delivery is a key component in the performance of any therapeutic. Providing active pharmaceutical ingredients (APIs) to a target in appropriate doses poses a myriad of interdisciplinary challenges; even miniscule changes can result in reduced therapeutic efficacy, poor manufacturability, or, at worst, potentially life-threatening side effects. Computational materials science can contribute important information relevant to the physicochemical properties of an API and its solid form. These techniques allow researchers to explore the molecular level processes that underpin these observed bulk phenomena to minimize potential downstream risk. As a result, teams can feel confident that they are providing the most efficacious and safe products to their patients.

DASSAULT SYSTEMES

MITIGATING RISK FOR DRUG DEVELOPMENT

Today's R&D departments are facing increasing pressure to improve their productivity and bring higher quality therapeutics to market. For drug development, this means balancing a range of biological and physicochemical properties, such as specificity, potency, metabolism, solubility and stability. However, determining the physical properties of pharmaceuticals experimentally is expensive and time consuming. Limited supplies of APIs can also constrain the amount of testing that can be done. This can create significant risk, as insufficient characterization can lead to the release of poorly optimized compounds to the market. For example, an unknown crystal polymorph could significantly impact a drug's bioavailability: at best this could result in an ineffective medication; at worst it could lead to potentially life-threatening side effects. To mitigate this risk, researchers must explore alternative methods to improve the quality of their drug pipeline.

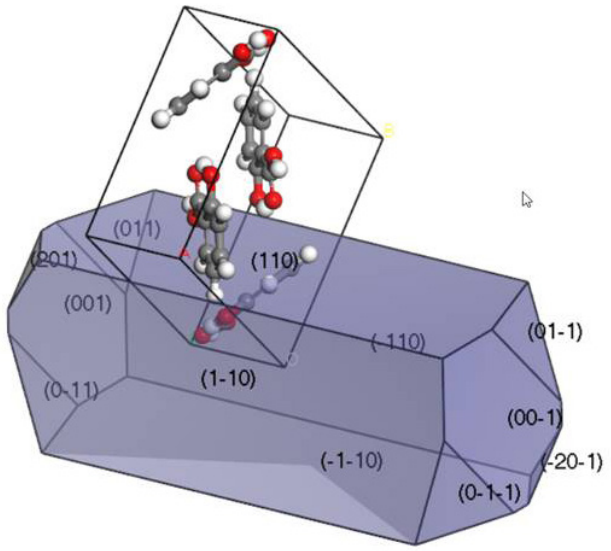


Figure 1. BIOVIA Materials Studio explores a variety of packing conformations of APIs to predict crystal morphology and growth

MATERIALS SCIENCE APPLICATIONS FOR PHARMACEUTICALS

Computational materials science techniques can help researchers gain a deeper understanding of the molecular interactions that underpin the physicochemical properties of a drug and its interactions with excipients and other coformers. BIOVIA Materials Studio offers a comprehensive collection of tools to foster the understanding researchers need to optimize existing formulations, develop new ones or explore completely novel delivery methods.

Crystallization and Morphology

A key component for determining the performance of an orally administered therapeutic is elucidating its crystal forms. These crystals may be pure forms of the API, be blended with multiple APIs, or be mixed with cocrystals and other excipients. Additionally, APIs may have several crystal forms – polymorphs. As a different crystal form can drastically impact the processability of the drug, it is critical to determine which are the most likely to form to optimize its manufacturability. Using an "*in silico* first" approach can help save valuable resources for the tests which are most likely to succeed and reduce development time.

BIOVIA Materials Studio provides a collection of tools for the prediction and analysis of crystal structures, allowing you to:

- Simulate powder diffraction spectra, index experimental powders and refine crystal structures against experimental data to determine crystal structures
- Explore potential polymorphs of a given compound directly from its molecular structure
- Predict the external morphology of a crystalline material from its internal crystal structure and determine the effects of solvents and impurities on the overall crystalline system

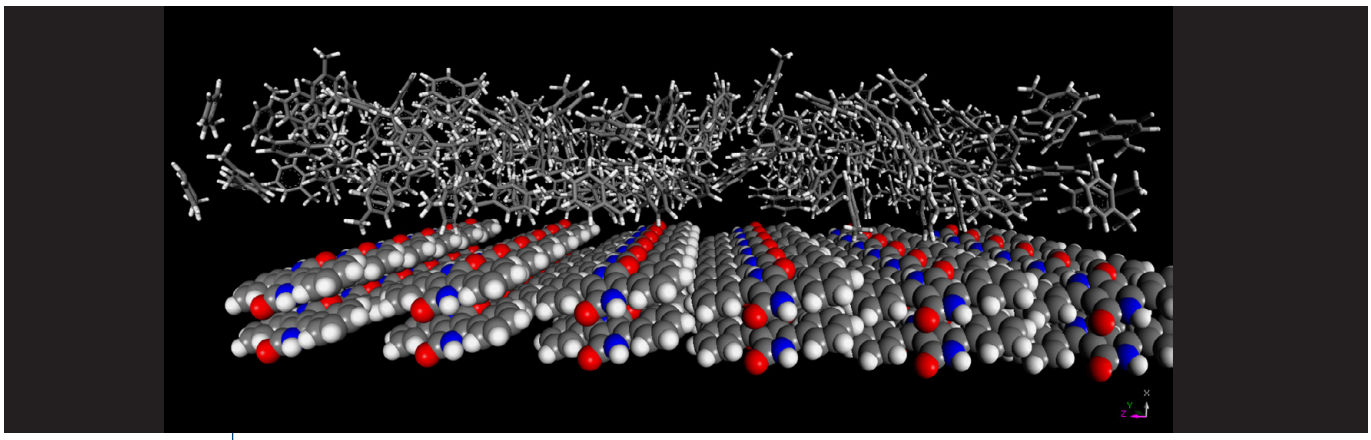


Figure 2. The interactions of toluene with a crystal surface, as modeled in BIOVIA Materials Studio.

Stability

Many therapeutics may sit on a shelf for a while before finding their way to a patient. As a result, ensuring that compounds retain their potency and not react with other excipients as well as the environment drives a significant portion of therapeutics development. Even retaining the aesthetic qualities of a pill throughout the product's lifecycle is key. However, many shelf stability studies are by their very nature time consuming. Additionally, as amorphous dosage forms increase in popularity, scientists must also consider other factors such as the solid's glass transition temperature.

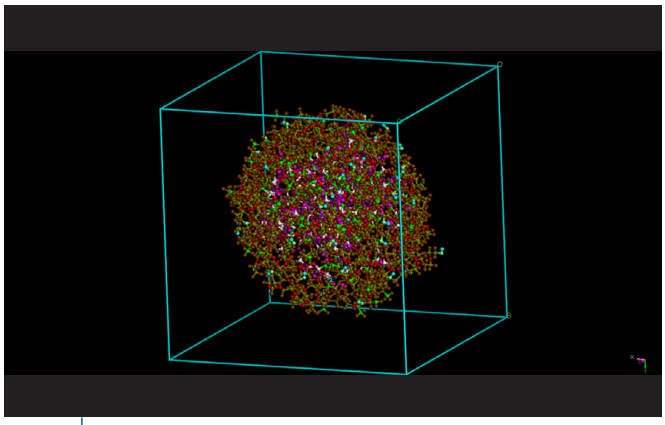


Figure 3. BIOVIA Materials Studio allows researchers to explore novel therapeutic delivery methods, such as nanoparticles.

With BIOVIA Materials Studio, researchers can:

- Ascertain the potential of candidate compounds for autoxidation or cross-reactions with various excipients
- Predict the glass transition temperature and other properties to explore the stability of candidate compounds in amorphous solid dispersion
- Determine mechanical properties of candidate compounds for manufacturability (milling, mixing, etc.)

Solubility

A major challenge in the design of many pharmaceuticals is poor water solubility. Researchers have a variety of methods to address this challenge, from chemical methods such as utilizing prodrugs or salt formation to physical methods like mixing drugs with cocrystals. Recently, new "carrier systems" such as micelles and microemulsions offer significant promise as a means to get a candidate therapeutic to its target. In addition to these approaches, researchers must have an understanding of the solubility of their compounds in water or – in the case of new carrier systems – other solvents.

BIOVIA Materials Studio, coupled with COSMO*therm*, allows researchers to explore a range of parameters that influence the solubility of their candidates.

- Carry out high throughput calculations of a variety of dispersion coefficients such as logD and AlogP
- Calculate solubility and miscibility parameters for compounds via simulation
- Predict compound solubility in various solvents and screen cocrystals
- Determine compound "loading" in micelles and other carrier systems

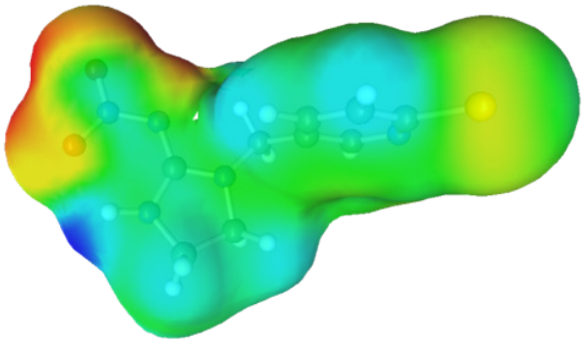


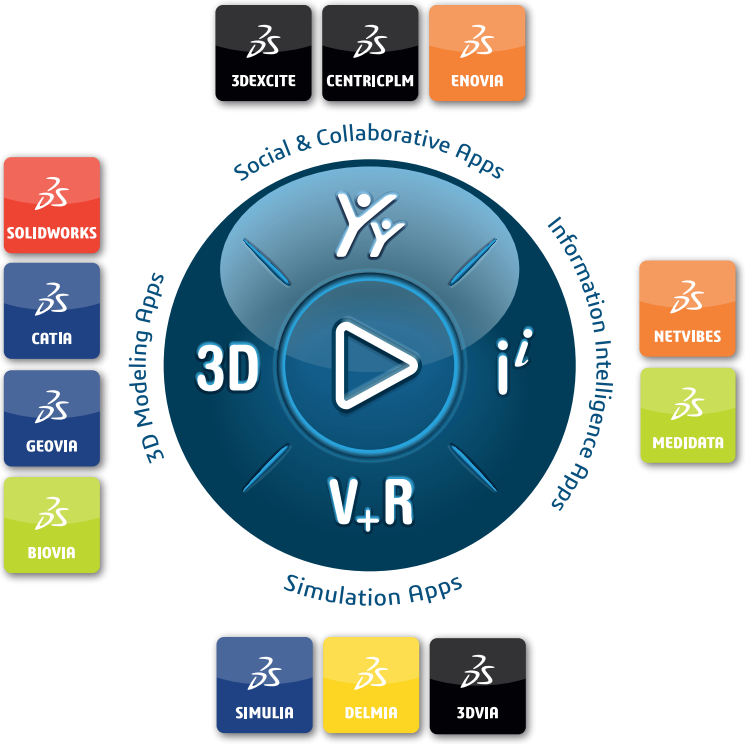
Figure 4. COSMO*therm* provides insight into the factors that influence a compound's solubility in a variety of solvents.

Manufacturing Optimization

Processing issues can also be investigated by understanding drug and chassis interactions at a molecular level. For instance, minimizing common problems during tablet production, such as sticking in the molds, can significantly decrease costs. With Materials Studio, you can measure adhesion at the tablet-mold interfaces to predict and mitigate mold sticking issues. By using this information with models from the wider Dassault Systèmes portfolio of simulation capabilities, it is possible to go further and build a virtual twin of the tablet production process, including the powder compaction into the tablet mold.

MATERIALS SCIENCE IN PHARMA: SAFER, MORE EFFICACIOUS THERAPEUTICS

There are a variety of factors that impact the performance of a candidate therapeutic. By adopting a more interdisciplinary mindset, researchers can optimize their treatments further upstream in the R&D process, ensuring that increasingly high quality candidates matriculate down the pipeline. Additionally, a deeper understanding of the materials properties of a compound can open up previously inaccessible compounds to new delivery systems. BIOVIA Materials Studio, coupled with the broader BIOVIA portfolio that includes deep capabilities supporting physical testing workflows can help bridge the gap between virtual and real experimentation. Together these capabilities can help foster the understanding that researchers need to develop the high quality treatments required to improve patient quality of life today and tomorrow.



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