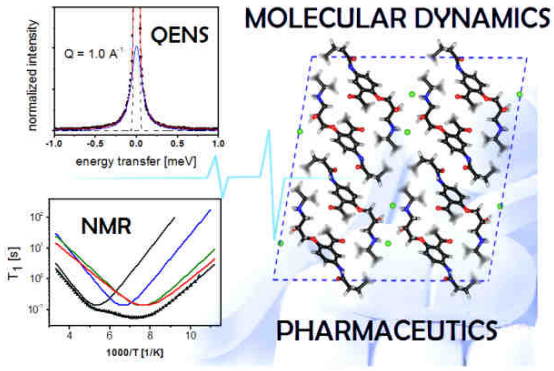
MOLECULAR DYNAMICS IN ACTIVE PHARMACEUTICAL INGREDIENTS

Faculty of Physics

COMPLEMENTARY SPECTROSCOPY TECHNIQUES

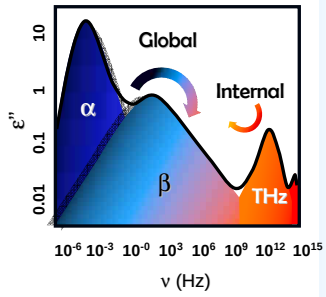


Understanding the mechanisms underlying the behavior of active pharmaceutical ingredients (APIs) is one of the greatest challenges for modern pharmaceutical science. The dynamics of molecular entities and their fragments at a different time scale is important for substrate-receptor interactions, for the drug metabolism in a cell as well as for the phase stability of a solid form of an API. The latter factor is crucial for pharmaceutical industry, being related to drug solubility, which determines oral-bioavailability of active pharmaceutical ingredients.

At the Department of Radiospectroscopy we combine a variety of experimental techniques with the state-of-the-art theoretical calculations in order to explore, understand and improve the structure and behavior of molecular pharmaceutics in crystalline and amorphous (glassy) states.

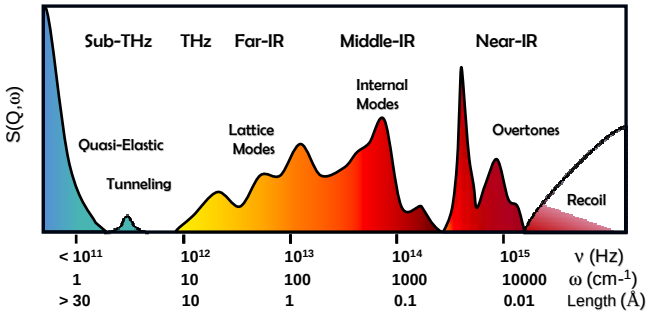
MOLECULAR DYNAMICS AT A DIFFERENT TIME SCALE

GLASSY DIELECTRICS

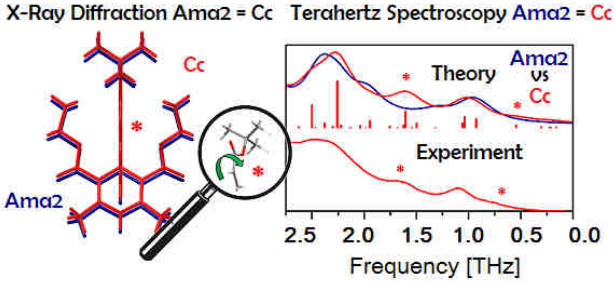


Molecular dynamics can be related both to mobility of whole molecular entities (global), usually observed in amorphous state, as well as to internal (local) mobility of molecular fragments. Internal dynamics of APIs is our main interest. We use a manifold of experimental techniques to observe the molecules in motion at a different time scale. To this end neutron (QENS, INS) and optical spectroscopy (THz-TDS, IR, Raman) along with NMR experiments and MD simulations are used.

NEUTRON SPECTROSCOPY



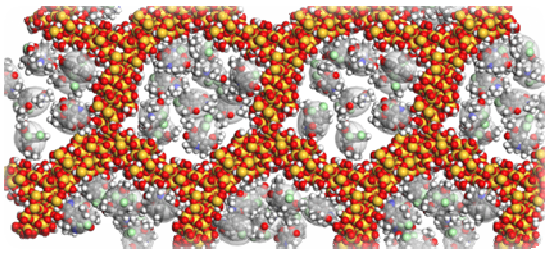
EXPLORING STRUCTURE AND DYNAMICS OF PHARMACEUTICAL DRUGS



A proper description of the crystal structure in a given polymorphic modification is an essential step in the FDA drug approving process. Moreover, it often seems that the number of discovered drug polymorphs is proportional to the time and money spent looking for them. We study the crystal structures of drugs and we develop combined experimental and theoretical protocols to improve characterization of pharmaceutical solids. Terahertz spectroscopy is an emerging experimental technique allowing for an efficient polymorph screening and description of subtle trails of molecular dynamics, which are inaccessible to other techniques. We successfully combine optical and neutron terahertz spectroscopy with solid-state density functional theory (DFT) computations.

APPLIED RESEARCH: BIOAVAILABILITY ENHANCEMENT

A huge part of the approved APIs is distributed as pills. The molecular interactions stabilizing molecules in a crystal state usually result in poor drug solubility and, hence, in a poor accessibility of an API to an organism (bioavailability). This can be improved by modifying the drug formulation, with an API transformed to a metastable state (confined, amorphous). Our team works on developing novel drug formulations. We use mesoporous silica and polymers as drug carriers, which lead us to considerable enhancement of drug bioavailability. The dynamics and interactions of confined APIs are studied by successful combination of neutron spectroscopy, NMR relaxation and classical molecular dynamics simulations.



DEPARTMENT OF RADIOSPECTROSCOPY

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