One estimates that the number of stable molecules that can be constructed from only C, N, O, H and S atoms amounts to more than $10^{60}$, of which only a tiny fraction is known. This astronomically large set of compounds spans the so-called chemical compound space (CCS). When one searches for novel molecules exhibiting some desired characteristics, one needs to screen the CCS until new, suitable and improved molecular structures are found. This resembles finding a needle in a haystack unless one applies clever search strategies.

The research described in this thesis focuses on Inverse Molecular Design strategies. Instead of starting from a (newly proposed) molecule and investigating its properties, we let the desired property guide the search by optimizing it as a function of the chemical structure. This inverse approach could deliver an important aid in the discovery of new valuable compounds, as such reducing the timescale of drug and materials development. More specifically, this PhD is oriented towards the optimization, acceleration and application of different inverse design methods.

Two general inverse design strategies are exploited. The first strategy concentrates on relatively small-sized chemical spaces defined by a fixed molecular framework on which certain chemical fragments can be substituted by others. Finding the best combination of structural fragments for this molecular framework is an optimization problem that can be solved effectively by discrete optimization algorithms, in particular the Best First Search (BFS) algorithm. In this work, several aspects of these algorithms are optimized to avoid local optima and to reduce the computational cost.

The improved algorithms were applied to diamondoids (nano-diamonds) and pentacene derivatives, both having potential as semiconductors.

The second strategy is to search through chemical space by a stochastic method that samples much larger regions of CCS, as such removing the constraint of a fixed molecular framework on which certain chemical fragments can be substituted by others. Finding the best combination of structural fragments for this molecular framework is an optimization problem that can be solved effectively by discrete optimization algorithms, in particular the Best First Search (BFS) algorithm. In this work, several aspects of these algorithms are optimized to avoid local optima and to reduce the computational cost.

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The property-optimizing ACSESS algorithm, which inversely designs molecules by an iterative procedure of repeatedly making random mutations and selecting the best and most diverse subset. We used the ACSESS algorithm, which inversely designs molecules by an iterative procedure of repeatedly making random mutations and selecting the best and most diverse subset. The property-optimizing ACSESS method was finally applied to find highly redox-active molecules for aqueous organic flow batteries using either quinone derivatives or stable radicals.

As a result, quinone derivatives with high reduction potentials were designed showing large aromatic stabilization of the reduced form and also a method to efficiently assess the radical stabilities was devised.