

# Journal of Business Chemistry

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The academic journal for management issues in the chemical industry

Jens Leker and Hannes Utikal

**The focus of the Journal of Business Chemistry: Good management practices in the chemical industry**

Interview with Hariolf Kottmann

**Managing growth and profitability in the chemical industry**

Alexander Kulesza, Kenta Stier and Marek P. Checinski

**High speed development of new chemical synthesis and materials at molecular-level: Methods and approaches**

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The Journal of Business Chemistry (JoBC) focusses on current developments and insights at the intersection of management and chemistry, biotechnology or pharmacy.

The JoBC provides an international forum for researchers and practitioners in companies, research institutes, public authorities, consultancies or NGOs to present and discuss current challenges as well as potential solutions in an interdisciplinary manner. Thus, the JoBC aims to foster the dialog between science and business, to support management practice in the chemical and pharmaceutical industry and to indicate where further research from academia is needed. The JoBC offers high quality publications with academic standards, a fast publishing process and global reach. With this multidisciplinary and boundary-spanning approach, the Journal of Business Chemistry intends to become the leading journal for decision makers in the chemical and pharmaceutical industry.

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The Journal of Business Chemistry (ISSN 1613-9623) is jointly published by the Institute of Business Administration at the Department of Chemistry and Pharmacy (University of Münster) and the Center for Industry and Sustainability (Provadis School of International Management and Technology). It is published every four months as an open access journal.

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# Letter from the Editors

## A new cooperation to advance the Journal of Business Chemistry

The landscape of the chemical, pharmaceutical and biotech industry has changed over the past years, not least due to mergers and acquisitions. Most prominent examples are Bayer's latest acquisition of Monsanto and the rumors about Dow and DuPont merging their businesses. Among the companies, which are not involved in M&A negotiations recently, the tendency to enter collaborations becomes visible. Just like actors in the chemical industry are searching for allies, the JoBC has found a new partner for publishing relevant content around current developments and challenges in the sector.

We are thus pleased to announce that the JoBC will from now on be jointly published by the Institute of Business Administration at the Department of Chemistry and Pharmacy (University of Münster) and the Center for Industry and Sustainability (Provdavis School of International Management and Technology, Frankfurt/Main). While maintaining our approach of presenting topics at the intersection of management and chemistry, new impulses will guide future contents of the JoBC.

We present our revised concept in the article "The focus of the Journal of Business Chemistry: Good management practices in the chemical industry" to our present and future community. The Editors-in-Chief Jens Leker and Hannes Utikal identify six challenges of the chemical, pharmaceutical and biotech industry emphasizing its importance as a research object for good management practice.

The interview "Managing growth and profitability in the chemical industry" with Hariolf Kottmann, the CEO of Clariant, focuses on specific management characteristics in chemical companies. Furthermore, the value of the organizational structure for successful management as well as current trend topics such as interdisciplinary and cross-industry collaborations and the 'smart industry' movement are discussed.

The article "High speed development of new chemical synthesis and materials at molecular-level: Methods and approaches" by Alexander Kulesza, Kenta Stier, and Marek P. Chęcinski presents the application of quantum chemical calculations in the chemical industry. The development of new simulation methods and technological opportunities (such as HTS) particularly enables research intensive industries to design their research more efficiently. As a consequence, the companies can achieve successful innovations in less time and by using fewer resources.

Please enjoy reading the third issue of the thirteenth volume of the Journal of Business Chemistry. We are grateful for the support of all authors and reviewers. If you have any comments or suggestions, please do not hesitate to contact us at [contact@businesschemistry.org](mailto:contact@businesschemistry.org).

Ruth Herrmann  
(Executive Editor)

Bernd Winters  
(Executive Editor)

## Commentary

# The focus of the Journal of Business Chemistry: Good management practices in the chemical industry

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The chemical industry is one of the major global industries with specific management challenges. It is an industry in transition. Compared with its economic importance and its role in providing solutions for grand societal challenges, this industry as well as companies from pharmaceutical and biotech sectors receive comparatively little attention from management literature. With the Journal of Business Chemistry, we intend to create an international platform for discussions between scholars and practitioners on good management practice in these sectors. We thereby promote an interdisciplinary and transboundary approach and encourage authors and readers to look at developments at the intersection of natural sciences and management.

The chemical industry affects all aspects of human life. Advances in chemicals and pharmaceuticals have contributed to improve living conditions, in particular through innovations in the area of health and nutrition worldwide. Progress in the automobile industry such as new developments concerning electric mobility were only made possible thanks to new materials and new formulations originating from the chemical industry. Also new electronic devices such as smartphones have only been made possible due to a change of pace in the development of electronic materials and an increase in their purity. Continuous research for and production of active pharmaceutical ingredients (APIs) are essential for fighting (new) diseases and improving therapeutic methods. From an economic perspective, the crucial role of the chemical industry is also reflected by its impressive size of more than €4,710 billion world chemicals sales in 2015 (Verband der Chemischen Industrie e.V., 2016), its average global growth rate slightly above the global gross domestic product (GDP), and an impressive growth in Asia. All of these characteristics make the chemical industry to one of the most fascinating industries, not only from a

scientific, technological or societal perspective, but also from a business point of view.

The Journal of Business Chemistry (JoBC) focusses on current developments and insights at the intersection of management and chemistry, biotechnology or pharmacy.

Our goal is to provide an international forum for researchers and practitioners in companies, research institutes, public authorities, consultancies or NGOs to present and discuss current challenges as well as potential solutions in an interdisciplinary manner. Thus, the Journal of Business Chemistry aims to foster the dialog between science and business, to support management practice in the chemical and pharmaceutical industry and to indicate where further research from academia is needed. With this multidisciplinary and boundary-spanning approach, the Journal of Business Chemistry is set to become the leading journal for decision makers in the chemical and pharmaceutical industry.

All articles focus on the chemical industry, including the biotechnology, pharmaceutical or process sectors in general. They are typically rooted in one

field (e.g. chemistry) and explore implications for others (e.g. management) or can stem from interdisciplinary research. The Journal of Business Chemistry publishes peer-reviewed research papers, essays from practitioners' perspective and commentaries. Research papers are based on empirical or conceptual research and advance the understanding of an important issue in the chemical (or a related) industry. Articles in the practitioner's section describe current developments in the chemical industry and share the lessons learned from practice. Commentaries are short statements regarding current research/ business problems or previous articles of the Journal of Business Chemistry. They mainly reflect the author's personal opinion and should encourage scientific discussion. It is our intention to catalyze the reasoning in good management practices in the industry in this phase of industry transition and to foster the dialogue between academia and practice.

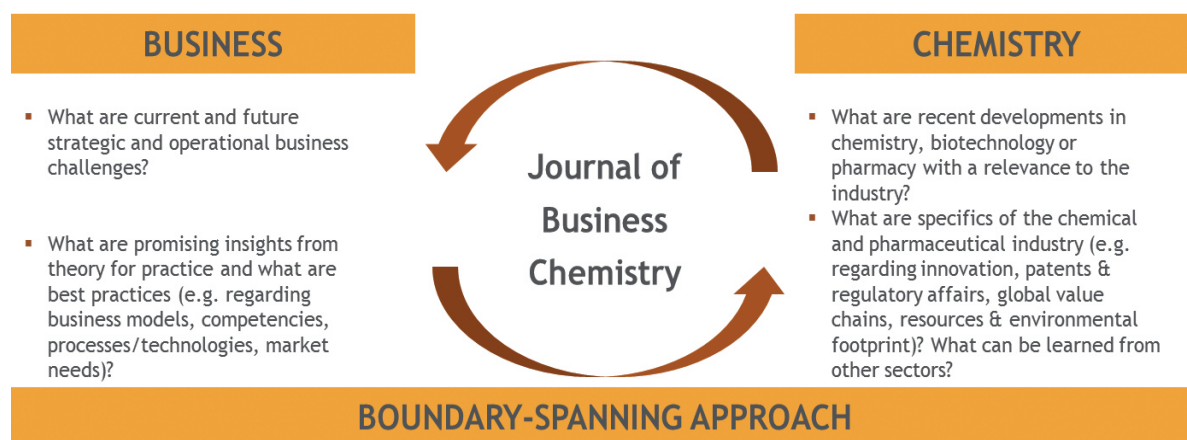
In the following, the chemical industry – encompassing in our definition companies from the chemical, pharmaceutical and biotech industry – will be characterized with regards to selected aspects influencing management decisions. Starting with the commonalities of the chemical, pharmaceutical and biotech industry, the Journal of Business Chemistry also aims to take the difference between these sectors into account. In the following, six topics are depicted and presented in more detail, along with their influence on management decisions in the chemical industry.

Firstly, the chemical industry is profoundly char-

acterized by **underlying basic research**. Alfred Chandler, a business historian, states that the success of chemical and pharmaceutical companies resulted in the past from transferring basic research findings into marketable products. Furthermore, he stated that in the past successful companies invested the profits and learning from each product generation to commercialize the next generation. Summarizing this pattern in one expression he called this capability the „engine of success“, which implies that in the past, inventions from the academic discipline of chemistry led to economic success of companies in the chemical industry. Nowadays, however, companies operating in the chemical industry need to wake up to the fact that chemistry as a science has stopped being the driver of innovation and growth. Nowadays, incremental product and process developments are more importance important for successful companies in the chemical industry than basic research. Also, the success model of pharmaceutical companies developing new products based on basic research findings (blockbuster products) has faltered. Nevertheless, since the 1960s and 1970s, biology as well as related disciplines such as microbiology, enzymology and the beginnings of molecular biology contributed to generating new pharmaceutical products. Since the 1980s, advances in the field of biotechnology have fueled the development of innovative products from basic research findings.

Given these developments, the chemical industry is no longer exclusively characterized by developments in the academic field of chemistry. The future of the industry will depend to a very high degree on its ability to integrate findings from other

Figure 1 The Journal of Business Chemistry focusses on current developments and insights at the intersection of management and chemistry, biotechnology or pharmacy.



academic disciplines and to cooperate with other industries. Companies therefore need to abandon the beaten track. These developments profoundly influence managerial decisions in the field of strategy, technology and innovations management. Consequently, all parts of the company (all business functions, the necessary skills of employees and the companies' corporate culture) are affected by this change. The chemical industry is thus an industry in transition, relying on a greater range of academic disciplines and with increasing emphasis on cooperation with other industrial sectors. The Journal of Business Chemistry strives to publish articles reflecting these developments and resulting implications for managers and academia (Whitesides, 2015; Chandler, 2009; Schröter, 2007).

Secondly, the chemical industry is a **process industry** where firms “add value to materials by mixing, separating, forming, or chemical reactions”. Process industries differ from so-called discrete industries with regard to the production process. In discrete industries, e.g. the automotive or engineering industry, production pathways converge as final products are assembled by using multiple discrete input components. In contrast, a product in the chemical industry can simultaneously act as an intermediate, processed further to synthesize other products, or serve as a finished, salable product. Production processes can therefore be convergent and divergent at the same time, which increases the complexity of planning and optimizing such processes. In each process, components are mixed and react under well-defined physical conditions. Technological characteristics in the “technical core” of companies in the chemical industry set the frame for all managerial decisions. For companies in the basic chemical sector, production processes need to be stable and optimized for high quality product generation. The need to build up capital-intensive production facilities inhibits the “agility” and “flexibility” of companies in this sector. In contrast, the pharmaceutical industry with batch production can be more flexible. The degree to which companies are flexible highly depends on the kind of production process implemented. Managers in chemical, pharmaceutical and biotech companies are thus bound by process characteristics and cannot easily transfer “management insights” from other industries. The Journal of Business Chemistry seeks to publish cutting edge research on the impact of technological requirements on management decisions (Wallace, 1984; Kannegiesser et al., 2008).

Thirdly, the **relations towards the market** are different in comparison with other industries: the chemical, pharmaceutical and biotech industries

are made up of a myriad of different products and markets. The importance of “business to business” versus “business to consumer” marketing varies across the three sectors: Business to business markets are of very high importance to companies in the chemical industry. Many of the products are used in industrial production, sold to other companies, or used within the same company in a separate production process. The biotechnology industry also relies very heavily on business-to-business income. Through their structure of licensing agreements they are very closely interlinked with other firms. On the other hand, the pharmaceutical industry must market its products to the medical profession and the public, where characteristics of business to business as well as business to consumer markets often prevail (especially in the field of “over the counter products” sold in pharmacies). Overall, the chemical industry has a mixed profile of market relations, developing products for industrial processes and agriculture as well as for the general public. For the Journal of Business Chemistry this implies that aspects of marketing and supplier-customer-relations need to be analyzed in a highly differentiated manner, taking into account the specifics of the different segments (Kortmann and Piller, 2016).

Fourthly, companies in the chemical industry highly depend on **non-renewable resources** such as fossil fuel as input factors for their production processes and on heat and electricity made from coal, gas or oil. Substitutes for these limited raw materials and energy sources are of strategic importance for companies in the chemical industry. In addition, chemical products affect the ecological footprint of all final products that are to a greater or lesser extent made up of chemical products. The combination of chemicals included in production processes at all stages of the value chain influences opportunities for product recycling. The chemical industry is therefore strongly affected by the idea of a circular economy. Activities at different stages of the value chain are seen in their interdependencies and closed loops for using and reusing materials are created. Applying this idea of a circular economy to the chemical industry provides opportunities for product, process and business model innovation. The analysis of linkages between chemical companies and their suppliers, their customers and the final consumption processes is a prerequisite for realizing benefits of the circular economy idea. The implications of the circular economy paradigm for chemical companies and their innovation activities will be another major topic for the Journal of Business Chemistry (Lieder and Rashid, 2016; Jenck et al., 2004).



Fifthly, the chemical industry is a **global industry**. Geographically, the chemical industry affects at least three different markets. The global footprint is determined by production, raw material and energy costs on the one hand, and the need to guarantee immediate market access on the other. For a very limited number of products, companies produce the entire global supply at one location. In this case, transportation costs must be negligible in view of the total cost of a good and economies of scale. As a consequence, consolidation of production in one plant is preferred over a global duplication of production activities. This is particularly valuable for producing APIs where production processes typically have to be accredited. Nevertheless, regional production for the European, North American and Asian market is pursued for the majority of products. While there are limited trade flows between these main manufacturing regions, trading within the regions, e.g. within the European Union, is more intense. In addition to global and regional markets, local markets can also be identified, where products are only delivered around or even within one specific production facility. This can be observed in a so-called Verbund (combined) production system. Such a system is characterized by an integrated production where products are, via pipes, directly delivered to customers based at the same location via pipes. Industrial parks where distinct companies use one common infrastructure are an additional pattern of organizing chemical companies. Overall, the chemical industry occupies a multiregional role. Managerial questions related to this characteristic focus on the question of how to handle opportunities and risks related to centralizing and decentralizing activities for a company as a whole and for its different business functions. How close should the company be to its lead markets? How should learning and innovation processes be organized? How can a chemical company with the need for capital-intensive production facilities exploit market opportunities in a growing emerging market – and how can volumes be adjusted if the emerging market has growth problems? To what degree is the concept of the “agile enterprise” applicable to companies in the chemical industries? These issues will be analyzed by both management scholars and practitioners in the Journal of Business Chemistry (Hofmann and Budde, 2006; Cesaroni et al., 2007).

Sixthly, companies from the chemical, pharmaceutical and biotech sector have to manage a very broad range of **stakeholders** in order to secure their “license to operate”. Companies from all three sectors may help solving societal challenges (e.g. by providing nutrition to a growing global population or by providing drugs against illnesses). At the same

time, they have a very high impact on the ecological environment and receive much attention from different societal actors (e.g. civil society, politics, customers, suppliers). Some topics related to the three industries, such as genetically modified organisms, animal testing and pricing of pharmaceuticals, are inherently controversial in the public domain. Furthermore, the chemical industry in particular looks back on a history of sometimes pervasive environmental accidents. The biotechnology industry has inherent ethical dilemmas because it, by definition, deals with living organisms by definition. Business ethics and issues regarding environmental and social sustainability are pertinent to the chemical and pharmaceutical industry as they need consumer support and trust to market their products. Thus, important tasks for companies in all three sectors are to (a) understand and manage a variety of stakeholders, (b) integrate the concept of sustainability in their strategic management processes and to balance requirements from economic, ecological and social perspectives, (c) to position an individual company as a “responsible societal actor” in the public domain. These topics are also featured in the Journal of Business Chemistry (Henderson, 2015).

## Topics of interest

The chemical, pharmaceutical and biotechnology industry is characterized by their its changing environment, as mentioned above. The Journal of Business Chemistry focusses on the developments in the chemical industry and encourages scholars to submit papers highlighting management specifics of these industries or comparing these industries with other important industrial sectors. At the same time, the Journal would like to invite practitioners to share their insights on successful management practices.

In the following some relevant topics are listed:

- strategy, innovation and technology management (e.g. interdisciplinary innovation; cross-industry collaboration; business model innovation),
- process optimization and digitalization (e.g. with an focus on production processes; sales processes; value networks),
- sustainability, green chemistry and the circular economy
- competencies for employees (e.g. technical expertise, social skills, and „transition competencies“)

The Journal of Business Chemistry is looking forward to discussing authors’ and readers’ perspectives on the future of the chemical industry, an industry in transition. Together with all relevant



stakeholders, the Journal hopes to strengthen the academic field of “successful management in the chemical industry” in a way that is relevant to practitioners. Furthermore, the Journal believes that our interdisciplinary (“business meets chemistry”) and boundary spanning (“academia meets practice”) approach will create benefits for all actors involved.

*agement terminology and phrases*, 5th ed. American Production and Inventory Control Society, Falls Church, VA.

Whitesides, G. M. (2015): Reinventing chemistry, *Angewandte Chemie International Edition*, **54** (11), pp. 3196-3209.

---

## References

Cesaroni, F., Gambardella, A., and Mariani, M. (2007): The evolution of networks in the chemical industry, in: Galambos, L., Hiniko, T., and Zambagni, V., (eds.), *The Global Chemical Industry in the Age of the Petrochemical Revolution*, Cambridge University Press, Cambridge, pp. 53-80.

Chandler, A. D. (2009): *Shaping the industrial century: The remarkable story of the evolution of the modern chemical and pharmaceutical industries* (Vol. 46), Harvard University Press.

Henderson, R., Gulati, R., and Tushman, M. (Eds.). (2015): *Leading sustainable change: An organizational perspective*, OUP, Oxford.

Hofmann, K., and Budde, F. (2006): *Today's Chemical Industry: Which Way Is Up?*, Wiley-VCH, Weinheim.

Jenck, J. F., Agterberg, F., and Droescher, M. J. (2004): Products and processes for a sustainable chemical industry: a review of achievements and prospects, *Green Chemistry*, **6** (11), pp. 544-556.

Kannegiesser, M., Günther, H. O., Van Beek, P., Grunow, M., and Habla, C. (2008): *Value Chain Management in the Chemical Industry - Global Value Chain Planning of Commodities*, Physica, Heidelberg.

Kortmann, S., and Piller, F. (2016). Open Business Models and Closed-Loop Value Chains, *California Management Review*, **58** (3), pp. 88-108.

Lieder, M., and Rashid, A. (2016): Towards circular economy implementation: a comprehensive review in context of manufacturing industry, *Journal of Cleaner Production*, **115**, pp. 36-51.

Schröter, H. (2007): Competitive Strategies of the World's Largest Chemical Companies, 1970-2000, in: Galambos, L., Hiniko, T., and Zambagni, V., (eds.), *The Global Chemical Industry in the Age of the Petrochemical Revolution*, Cambridge University Press, Cambridge, pp. 53-80.


Verband der Chemischen Industrie e.V. (2016): Branchenporträt der deutschen chemisch-pharmazeutischen Industrie, VCI, Frankfurt.

Wallace, T. F. (1984): *APICS dictionary: the official dictionary of production and inventory man-*



## Interview

# Managing growth and profitability in the chemical industry



### Interview with Hariolf Kottmann, Chief Executive Officer (CEO) of Clariant\*

\* Clariant International Ltd., Hardstrasse 61, 4133 Pratteln, Switzerland, [www.clariant.com](http://www.clariant.com)

Since 2008 Hariolf Kottmann, holding a PhD in organic chemistry, is Chief Executive Officer of the Swiss specialty chemical company Clariant.

The corporation is headquartered in Basel and is operating in 53 countries worldwide. In 2015, Clariant occupied 17,213 employees of which around 1,100 (6.4%) are working in R&D. By focusing on the four business areas care chemicals, catalysis, natural resources, and plastics & coatings, the company generated sales of CHF 5,807 mn.

The JoBC team interviewed Hariolf Kottmann about his perceptions regarding challenges for management as well as current developments arising from the chemical industry.

**JoBC:** *Mr. Kottmann, what do you think makes management in the chemical industry specific?*

**Kottmann:** In the first instances the chemical industry is based on the same management principles like other industries. But to a certain extent our industry has to consider some characteristics – like the high R&D investments, the dependence on fossil resources, the energy intensity as well as the fact that the chemical companies are highly influencing their ecological and social environment. These factors may not have the same importance for companies of other industries. Furthermore, the cycles of new product developments are long-term oriented. This means that the establishment of new product capacity as well as supply chains takes more time compared to other industries. At the same time our industry faces volatile markets – what has been highly specialized chemistry yesterday, is nowadays mass production. These characteristics of the chemical industry indeed require optimal strategies developed by management.

**JoBC:** *Considering Clariant's 'period of extensive restructuring' over the past years, how decisive is the organizational structure for successful management?*

**Kottmann:** The organizational structure is the fundament of every company. If the structure does not support the company in doing business, there is something wrong. At Clariant we recognized the need to change and took action. The change of the organizational structure was driven on management level. Thereof, we had the chance to shape the organization in a manner, which ensures optimal communication throughout the whole organization. It was a long process to change the patterns of our organization, nevertheless it paid off at the end. Clariant reinvented itself by overcoming the established structures and is today one of the most successful companies shaping the industry of chemical specialties.

**JoBC:** *Continuing with the interdependence of management and organizational structure: How is this affecting the corporate's strategy and business activities, regarding for example the production or the R&D?*

**Kottmann:** As a company in the chemical specialty industry, you must be able to react with increasing flexibility and speed to global changes. The growth market of today can be the crisis market of tomorrow – just think of what we're experiencing in Brazil. What counts is a lean, flexible organization enabling our management to make the right decisions.

On top of that, you must succeed in responding equally to the specific wishes and needs of both your customers and other stakeholders. Depending on the market, customers of the chemical industry expect our products to give both them and their end customers a competitive edge. As a rule, we as a specialist chemical company deliver products and solutions that are processed further by other chemical companies. It is therefore vitally important for us to have locally based corporate activities such as research and production in addition to marketing and sales. Only then can we analyze the market accurately and register trends and needs that

may exist only there.

This is especially important from a management perspective. For example, to meet this challenge and deliver exactly the right solutions our customers want, we at Clariant have established a very clearly structured “idea-to-market” process. This includes customers, local contacts and our R&D experts right from the start.

**JoBC:** *Could you please explain the peculiarities for R&D & innovation in more detail?*

**Kottmann:** Our innovation is based on our analysis of megatrends, market developments and consumer needs. Together with our local customers, we develop ideas from the results. We speak to them and find out what problems they want to solve. Their requirements form the basis for the development of our innovations. We then develop a concept based on scientific standards that also comprises the delivery chain, the product registration and ensures the raw material supply.

And to make that possible everywhere, we have built up a worldwide R&D network. We have about 40 local “technical application centers” near our customers which are managed by the respective business units. This network is coordinated in Frankfurt-Höchst, where the “Clariant Innovation Centre” (CIC) acts as a sort of hub, a global competence center for chemical research, development and process technology.

**JoBC:** *What are you focusing on in the local centers?*

**Kottmann:** In Shanghai for example, we are building a center to concentrate on new catalysts that are specifically suitable for process technologies applied in China. In Brazil, a laboratory is currently being built to move ahead with applications for the cosmetic industry. It is specifically related to hair shampoo ingredients. Hair care is highly prized in Brazil, where the population structure is responsible for the greatest variety of hair types in the world. Consequently, it is of great importance to be present in the respective markets, without compromising the potential synergies.

**JoBC:** *Speaking of potential synergies, are interdisciplinary and cross-industry innovations valued and already part of Clariant's daily business?*

**Kottmann:** Absolutely, although the potential is more important than the volume. One example is Open Innovation. We have gained initial experience here, for instance in the area of functional packaging. We developed our Open Innovation Ini-

tiative jointly with the University of St. Gallen and Stanford University. The goal is the active and strategic integration of external knowledge into the company. We obtain this knowledge not only by using the generally available internet providers and our Open Innovation platform. We also actively invite external partners, start-ups or universities to contribute ideas and solutions to our Open Innovation focus fields. This results in the development of project-related, long-term partnerships. In return, we offer these partners access to financing opportunities, marketing, infrastructure and practical know-how. It's therefore a win-win situation for all concerned. I see great potential for this in the future.

**JoBC:** *There are further capabilities besides interdisciplinaryity which are highly demanded nowadays. Which challenges do you see especially in the area of employees' behavior as well as recruiting and education?*

**Kottmann:** In order to develop service and product offers beyond established value-adding chains, a company needs the corresponding know-how: in biotechnology, material sciences, process technology, information technology or nanotechnology. The classic professions – chemists, chemical engineers, but also commercial professions – continue to play an important role. However, the great challenge is to find appropriate experts on the labor market, because we are competing here for the best talents.

This is the reason why we practice employer branding. We must be able to communicate why our company offers better opportunities to people who want to develop themselves and become part of our innovative culture. Here again, what counts is not just expert knowledge, but rather openness for new ways of thinking. I am convinced that only an open corporate culture enables us to use the opportunities in areas of innovation.

A change of mind-sets that reflects the corporate culture is extremely important. There are still too many chemical bureaucrats - in our company too. To meet the challenges of megatrends and corporate change, we need a change of attitude and behavior, a cultural transformation from the center of the organization. We must all ask ourselves every day: What does my customer want? Where is the added value for him? What does that mean for me and my company? What contribution can I make? Along with Business Excellence therefore, the area of People Excellence has therefore a high priority for us.

**JoBC:** *The idea of sustainability is still challenging the chemical industry. Apart from developing the*

***right products, how could sustainability be supported by management?***

**Kottmann:** In our view, sustainability is an important motor of innovations generating additional growth. I am convinced that companies will in five years from now find it difficult to run their business successfully and remain socially accepted without taking account of sustainability. We have for instance established the “Portfolio Value Programme” initiative. This involves investigating our entire product range according to stringent sustainability criteria. If a product meets this test and shows an excellent sustainability profile, we identify it with our own EcoTain® label. Products in the range not meeting these demands are substituted.

We have furthermore introduced a sustainability index as an integral part of our Stage Gate process. This enables us to examine research projects at an early stage for compliance with sustainability criteria – a further measure to secure our long-term success.

Switching to renewable raw materials for selected applications is another of our objectives. We therefore rely increasingly on innovative products that can be derived from renewable raw materials in these areas.

One example is the production of surfactants from saccharides (sugars). We can use an intermediate stage in this process from bio-feedstock to end-product to develop, for instance, an innovative product that plays an important role in manufacturing paints and lacquers. This product is ideal for manufacturing odorless paints, which is particularly relevant for internal spaces. Because it is produced from renewable raw materials and does not harm aquatic organisms, it also has an outstanding environmental profile. This allows our industrial customers to use corresponding ecolabels for their end products, for example a lacquer you can buy in a DIY shop. This is becoming increasingly essential in the market.

***JoBC: Turning to another current trend, do you have an idea of how organizations will be affected by the ‘Smart Industry’ movement, also known as ‘Industry 4.0’?***

**Kottmann:** Digital technologies will influence the specialist chemical industry. They may not be as visible or as pioneering for us as for other sectors like the automotive or machine-building industries. But they will definitely affect us, starting with the growing transparency of, for instance, the flow of information or commodities along the value-adding chain. And digitalization will succeed in turning a customer’s requirements into entirely new busi-

ness opportunities reaching far beyond the actual products.

***JoBC: Which areas will be influenced by these developments?***

**Kottmann:** I can give you a current example from our Oil & Mining business unit: in oil production, plant operators and their suppliers are challenged by the wide distribution of the production facilities. The shale oil boom in the USA has created thousands of them. Visiting these sites and locally controlling the processes naturally demands much cost and effort expenditure. Oil production requires small volumes of special chemicals. Partners have helped us to develop software (VeriTrax analytics) that collects and automatically integrates key parameters and analysis data from the production plants and the corresponding laboratories, to which our engineers have direct access. They process the data and supply them to the laptops or smartphones of our customers. The key advantage is the combination of analysis and delivery. Veritrax Delivery identifies the production site via GPS data, computes the required amount of special chemicals and loads the order straight into the appropriate SAP system. This reduces data input and processing costs while increasing efficiency and quality at the customer’s end. And the field personnel does not need to climb into their pickups so often.

In this case, digitalization helps us to enter new terrain and differentiate ourselves from the competition. The example shows why we must constantly query our business approaches and consistently align ourselves towards customers and markets so that we do not miss such opportunities. It also has an influence on our employees. The issue here is a different way of working and the right attitude, which is why we are calling for a “change in mind-set”. Our basic and further training activities are also affected, and so is the way we approach potential employees.

***JoBC: Finally, how do you evaluate the current pressure to change in the chemical industry?***

**Kottmann:** To my mind, the constant change in our surroundings and the resulting consequences for specialist chemical companies are nothing new. Our global markets were and remain very dynamic and subject to continuous change. A company that seeks to be sustainably successful must therefore also change and develop permanently. Every company must keep asking itself what right it has to exist. We will not have earned our “license to operate” until we are able to explain to our stakeholders why our company should exist at all.

## Practitioner's Section

# High speed development of new chemical synthesis and materials at molecular-level: Methods and approaches

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Recent success of advanced computational chemistry, in example for the prediction of chemical reactivity and materials properties, reflects its reputation as a valuable and widely accepted means to tackle problems in academia. The development of new simulation methods and new computer architectures enables an enormous improvement of the productivity of research and development of new chemical synthesis and materials. These advances can be achieved in terms of less time, material, and staff compared to traditional lab experiments. Especially, approaches like virtual high throughput screenings (vHTS) are highly scalable and allow fast and deep insights into new promising system modifications. Consequently, the time to market and risk of new product development can be decreased significantly. These characteristics paved the way for the successful application in industry nowadays.

### 1 Introduction

The field of computational chemistry is diverse and offers a number of inherently different approaches suitable for different problems, targeting isolated molecules in the gas phase to extended solids, polymers and liquids. By simulating not only energy and derivative properties, but adding a time domain to the problem, the dynamics of the system of interest can be accessed. For research and development (R&D) projects, computational chemistry is an ideal tool to test new ideas for chemical transformations and new materials on the molecular level due to the fact that computations do not require synthesis or dedicated lab equipment. Furthermore, experimentally hard to characterize molecules - such as transient intermediates - can be investigated to full detail. In view of these benefits and the moderate investment costs for a specialized interdisciplinary team with own IT-Infrastructure (and no need for laboratory equipment), companies are able to generate a comparatively high return of investment (ROI) through developing new game-changing materials and synthesis routes (see a comparison of characteristics of traditional vs. computationally supported approaches in Table 1). This potential and value of

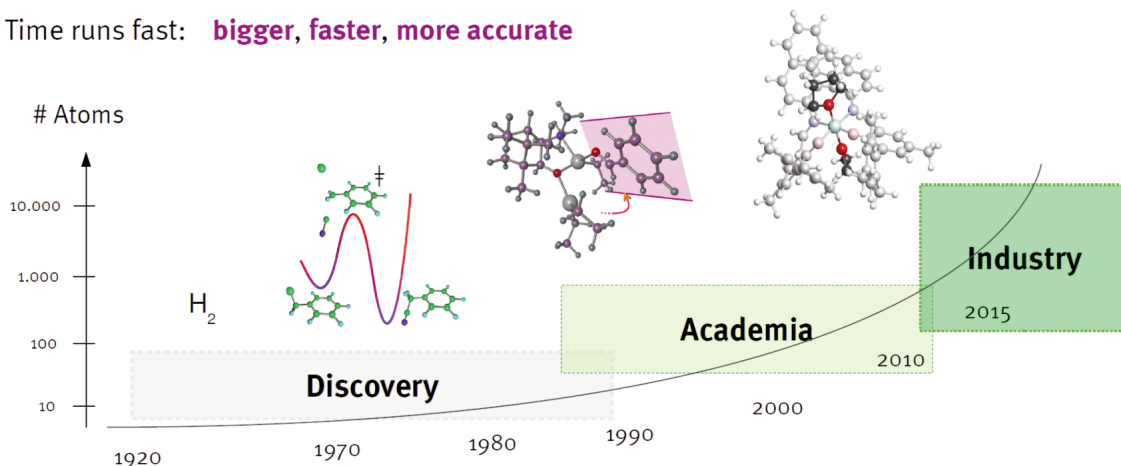
using computational approaches has already been pointed out in several industrial roadmaps (The American Chemical Society, 1996; Council for Chemical Research, 1999; Roadmap for Catalysis Research in Germany, 2010). The significantly increased number of molecules researched by computational chemistry is also schematically demonstrated in Figure 1.

From the vast field of computational chemistry, including multiscale descriptions, low-resolution, "coarse-grained" models and the broad field of classical molecular dynamics, this article focusses on describing techniques based on quantum mechanics providing universal descriptions of chemical transformations and materials as well as delivering key properties arising from the electronic structure that are not accessible with classical methods. In the following sections, an overview about the prospects and limitations of the technology is given and exemplary fields in which computational approaches have already been successfully applied and yielded in breakthrough innovations are presented. Selected methods and problems are used as showcases, e.g. to demonstrate how quantum chemical investigations can be utilized to analyze a) key steps of chemical processes, b) how strategies for the design of catalysts are adapted and c)



Figure 1 Simplified overview of the development of quantum mechanical simulations (number of atoms included in treatment vs. time). Examples from left to right depict potential energy surface exploration, rationalizing critical steps of selectivity, catalyst design, based on the simulations.

Time runs fast: **bigger, faster, more accurate**



how the identification of new materials can be accelerated.

### 1.1 Application of quantum mechanics: Synthesis

Improving the efficiency of chemical manufacturing processes leads to significant strategic advantages in highly competitive markets, which consequently enables companies to generate a higher added value. If the possibilities of cost reductions by optimizing the application of raw materials and energy supply are exhausted, increased process economy in form of higher production rates or higher product selectivity can be achieved by changing the process itself, additives (e.g. catalyst, ligand) or adjusting reaction conditions (e.g. solvent, temperature, process structure). Since the synthesis of chemical compounds can be a complex multi-step process during which different molecules interact within a particular reaction environment (e.g. solvent, catalysts, pollutants), adjustments of processes can be demanding.

Quantum mechanics offers the possibility to perform simulations for well-defined and designed model systems as well as for model problems picked by the researcher. The individual reaction steps and interactions, which are usually planned, performed and analyzed in laboratories, can thus be disentangled and examined separately and quantitatively without interference. Then, subsequently increasing the complexity of the simulations, influences of the individual reaction components on the whole process can be determined at the molecular level. In addition, the influence of process parameters

such as temperature, polarity and structure as well as solvent and concentration effects, which are known to have a high impact on the conversion and selectivity of reactions, can be investigated. In addition to stoichiometric syntheses, catalytic reactions can be studied by employing appropriate models for the active center of the catalysts (in fact, catalyzed reactions constitute the major part of chemical production). Using algorithms to search for critical points of the reaction path(s) such as the involved intermediate minima and their liaising transition states assembles a greater picture of the overall mechanism. Its analysis in terms of the energetics and entropic effects helps to determine why a reaction with one specific catalyst is faster and more selective than with a different one. Interpreting the molecular level findings on the process scale can provide evidence of why for example currently used production methods suffer from poor conversion or produce contaminated products, which need to be isolated at a high price. Due to the technically facile scalability of computations and number of mechanistic paths investigated, it is possible to examine a large number of molecular variations and reaction conditions in a short time compared to practical laboratory experiments (weeks instead of years). This saving in time allows for the parallelized exploration of process parameters: tailored to the chemical process and at the same time with high throughput. Table 1 compares the main characteristics of the conventional and extended approach.

The throughput of the computations can be further accelerated when using chemoinformatics



**Table 1** Comparison of the conventional and the computational approach. Abbreviations used in the table: Quantum mechanics (QM), semi-empirical quantum mechanics (sQM), molecular dynamics (MD), virtual high throughput screenings (vHTS), machine learning (ML), quantum mechanics derived force field (QMDFF).

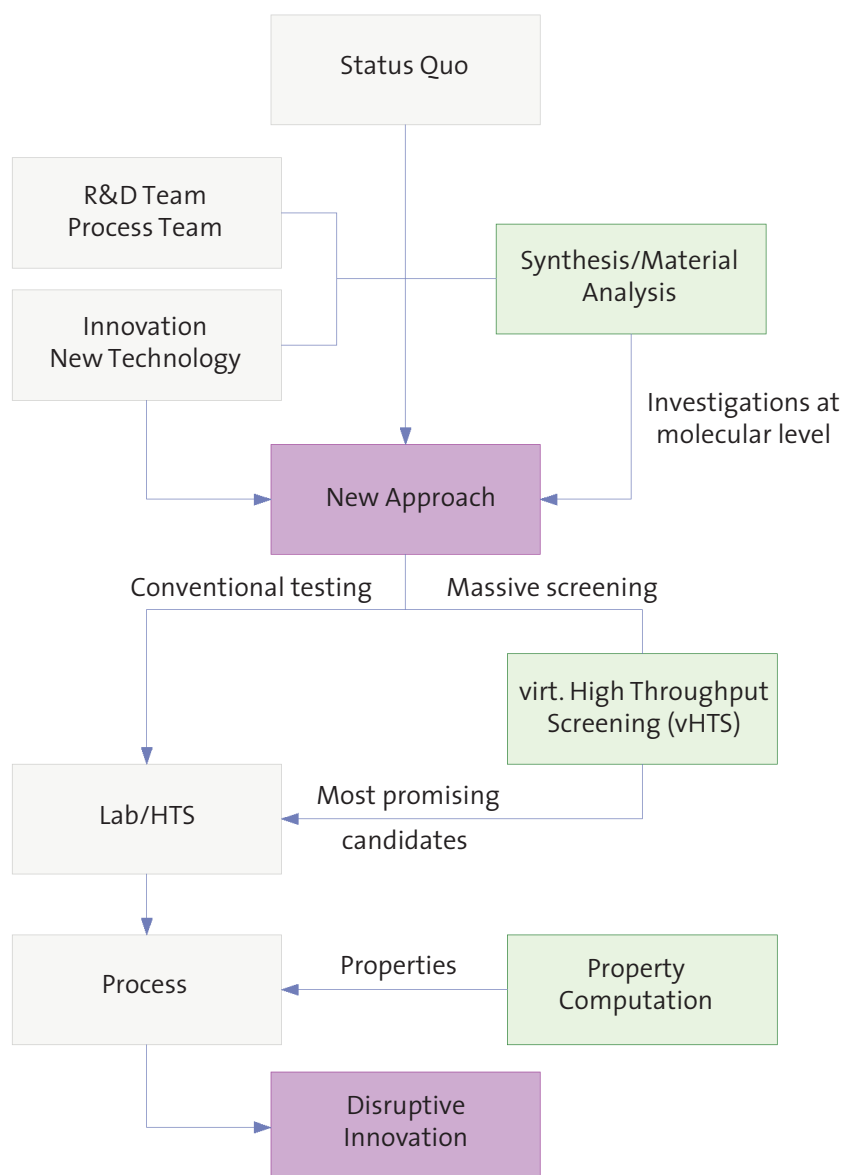
	Synthesis		Materials	
<b>General aim</b>	Activity & selectivity		Material properties	
<b>Specific target</b>	Activation barrier, deactivation, stability	Macroscopic effects (i.e. concentration temperature)	Molecular property (i.e. color, redox potential)	Macroscopic property (i.e. stability, viscosity)
<b>Conventional approach (Laboratory)</b>				
<b>Scalability</b>	5 - 100<		5 - 1000<	
<b>Time</b>	days - years		days - years	
<b>Staff</b>	5 - 50		3 - 50	
<b>Equipment</b>	Laboratories, chemicals, instruments for analytics, logistic, back office			
<b>Result</b>	better-or-worse, empirical hypotheses			
<b>Extended approach (Computation)</b>				
<b>Atomic scale</b>	Molecules, surfaces	Solutions, particles	Molecules, agglomerates	Solutions, polymers, particles
<b>Simulation approach</b>	QM/sQM	sQM	QM/sQM	sQM/(QMDFF)
<b>Process</b>	Mechanism analysis ↓ Determination of property influencing positions ↓ vHTS ↓ ML	Concentration, temperature, solvent ↓ MD ↓ Statistics	Determination of property influencing positions ↓ vHTS ↓ ML	Concentration, temperature, solvent ↓ MD ↓ Statistics
<b>Scalability</b>	10 - 10,000< reactions	10 - 100< reactions	10 - 1,000,000< molecules	10 - 100< materials
<b>Time</b>	days - weeks	weeks - month	days - weeks	weeks - month
<b>Staff</b>	3-5	2-4	2-5	1-3
<b>Equipment</b>	Advanced software and special computers			
<b>Result</b>	How much better-or-worse, explanations, global correlations, predictions			

concepts that use data mining and chemical databases techniques and allow high grades of automatization. The interaction with the vHTS scheme in an R&D project, together with a workflow is sketched in Figure 2. The presented example highlights that virtual high-throughput screenings (vHTS) may be used to investigate numerous new variations and to test in the computer model whether target parameters such as yield or selectivity can be improved. Consequently, the gained understanding of the trends in the reaction (espe-

cially the role of a series of modified catalysts) and the narrowing of the chemical variation space to only promising candidates greatly reduces development time and costs.

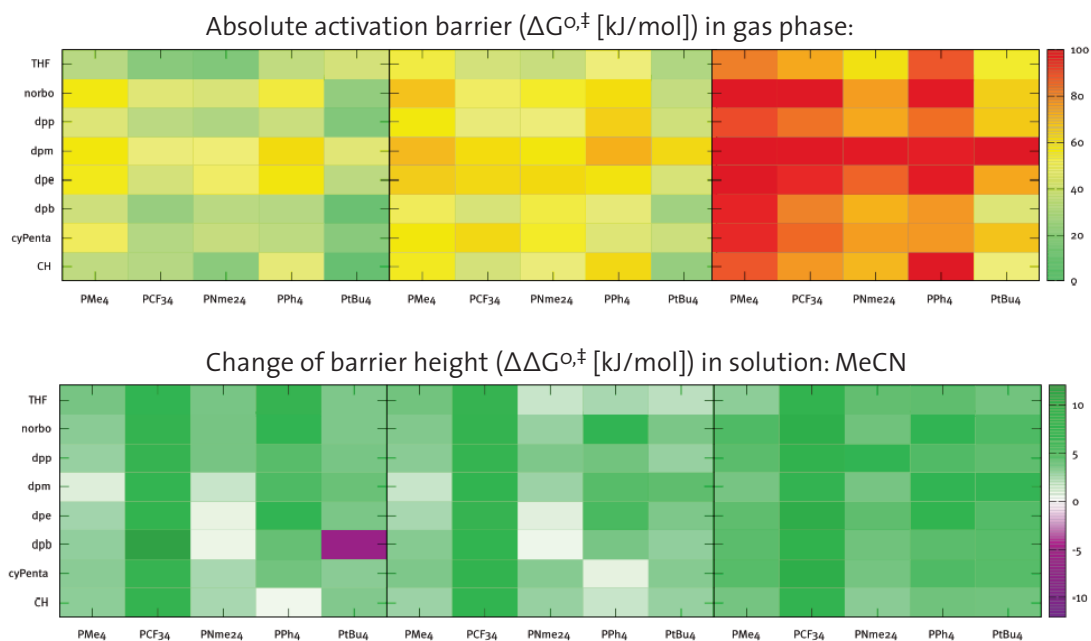
Figure 3 exemplarily shows a screening of the activation barrier of a CO insertion reaction, whereby the performance of several metals, ligand backbones, ligand rests, and solvents was evaluated. Homogeneous catalysts derived from Cole-Hamilton-type (metal-organic complexes) were taken as model catalysts. Different modifications were cre-

Figure 2 Comparing a conventional R&D process (grey) with a process involving the use of quantum mechanics and virtual high throughput screenings (green).



**Figure 3** Overview of a small virtual catalyst screening (vHTS) at the rate limiting step. Comparison of the activation barrier of different metals (Ni, Pd, Pt), ligand backbones and ligand derivatives. The impact of one solvent was also investigated (bottom).

### vHTS: Activation barrier



ated in-silico by changing functional groups of the ligands extremity (altering the bulkiness of the overall catalyst) and by changing the bidentate ligand's backbone length (altering the coordination geometry). The CO-insertion barrier was taken as descriptor that significantly contributes to the overall turnover frequency (TOF) of the reaction. For every member, this barrier was calculated at the DFT level (see below) and the height was color-coded. Green entries correspond to catalysts with high TOF – indicating potentially interesting leads for further testing. These quick evaluations thus show clearly which kind of metal, ligand backbone, and ligand rest combination is the most promising.

### 1.2 Application of quantum mechanics: Materials

The prospect to use theoretical methods to design and test new compounds in silico led to the idea of first-principles materials discovery (Curtarolo et al., 2013; Greeley et al., 2006; Maier et al., 2007). The necessary high-throughput computational screening (explanation see 1.1) of hypothetical chemical motifs or elemental compositions has indeed become more feasible in the recent past, given the availability of scalable high-performance computing infrastructure. Such pre-screening procedure

would reduce the R&D costs, where optimization potential of components for display dyes (Figure 4), batteries (Figure 5), sensors, electric circuits, photovoltaic devices etc. is expected by tuning the chemical structure and composition of the material itself. This can be achieved by choosing few promising backbones and create several derivatives of these structures. Compared to the research in laboratories, modern virtual high throughput screenings can examine much more structures in shorter time periods, at much lower costs and offering more results per molecule.

For new OLED emitter materials, one interesting question is to tune the color of the electroluminescence by chemical modification. In the example shown in Figure 4, modifications were done to an imidazole-derived compound displaying interesting photophysics. Known synthetically available modifications constitute the backbones HBPI, HPI, HPNI and NHPI to be further functionalized at position  $R_A$ . The screened descriptor is the emission wavelength obtained by a tailored semi-empirical excited state method after excited state relaxation. The values are coded to an RGB value for the visualization. The result from this screening is that only one backbone provides sensitivity to modification at  $R_A$ , while the others are relatively tolerant. Therefore, only the “sensitive” backbone might be cho-

sen for further treatment, since it covered a broad range of emission properties.

For the development of new organic battery materials, tuning the redox potential of a redox-active agent on the molecular level might be necessary. One interesting redox active organic motif is based on the tetrathiafulvalene (TTF) moiety. In the example screening in Figure 5, experimentally common functional groups are introduced in sili-

co at three positions to evaluate the impact of modification on the energetics of two oxidation steps (0/+ and +/++). The reference potentials (see black line) of the unfunctionalized molecule is systematically shifted to higher values as an outcome of the screening, which further allows to estimate the range of potentials addressable by this type of modification (the range covered by green and magenta sticks, respectively, for the two redox stages).

Figure 4 Screening of optical properties of several derivatives. Identification of the most important derivatives and position of a molecule backbone.

vHTS: Wavelength  $\lambda_{\max}$

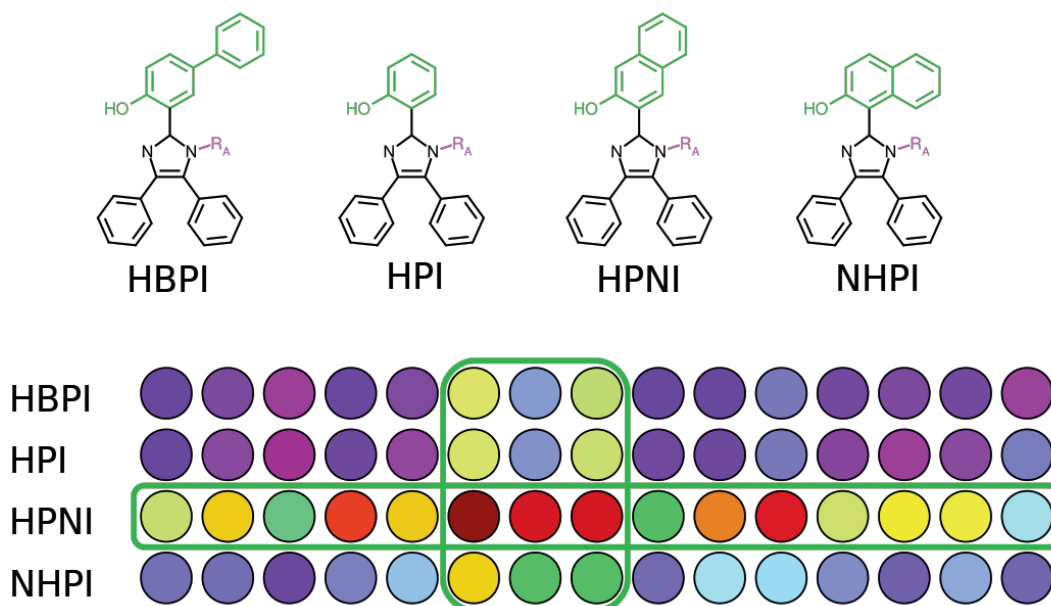
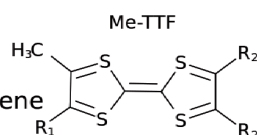


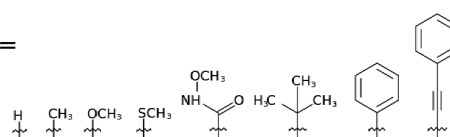
Figure 5 Virtual high throughput screening (vHTS) of new materials for organic battery applications. Distribution of the redox potential for 504 compounds in a few days.

vHTS: Redox potential

Functionalization of  
Methyl-tetrathiafulvalene



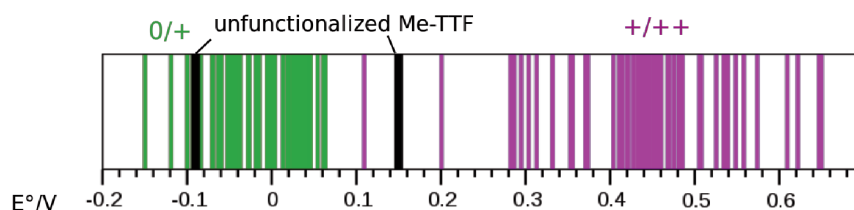
$R_{1,2} =$



8 times 8 configurations = 64 unique compounds

if  $R_2$  is not symmetric: = 504 unique compound

Range of accessible potentials:



Apart from the conduction of individual simulations within a screening, the time-evolution of the systems' structure can be simulated. With increasing computational power and advanced methodologies that allow quantum-level accuracy treatment with low computational costs, it is nowadays even possible to predict complex macroscopic properties like melting points or glass transition temperatures of any molecules or molecule mixtures with very low deviations to experiments. Figure 6 shows exemplarily the significant changes of the phase around the melting point or glass transition temperature, respectively.

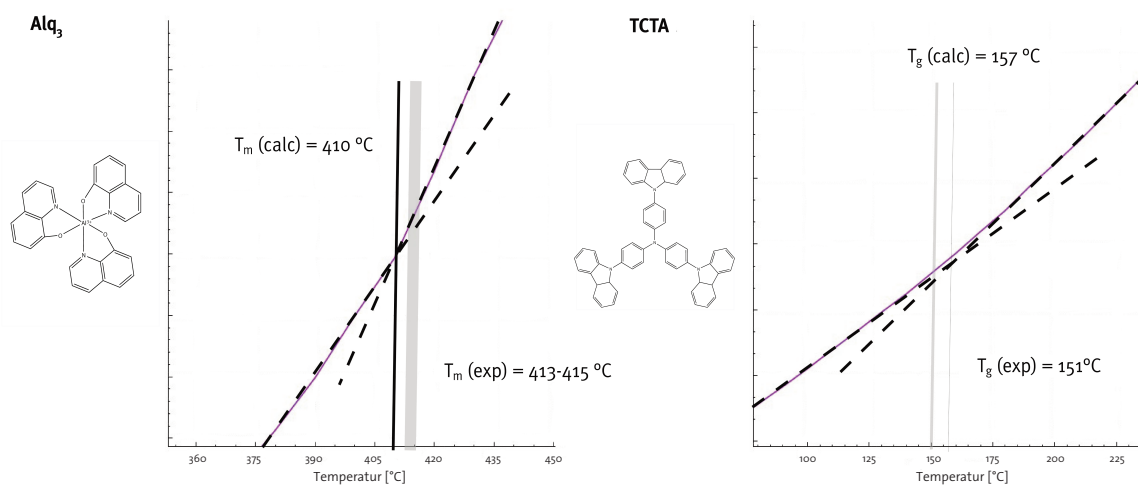
So far, also several industrial players made progress in establishing databases of predicted material properties (Jain et al., 2011). Despite the emerging technical feasibility of performing these screenings, their practical use in materials discovery in an industrial frame is limited so far. This limitation is mostly due to a discrepancy between the practical framework for the development of new materials in the R&D process characterized by safety regulations, costs, compatibility or durability requirement etc. and the rather limited prospect of a purely theoretically proposed formula to be ultimately successful. To picture an example, platinum metal is still frequently used as electrocatalyst in the hydrogen evolution reaction in water electrolysis, although several computational screenings have proposed materials of other elemental composition (Greeley et al., 2006; Andersson et al., 2006). However, a low number of abstract and simplified theoretical descriptors of the performance

are usually screened, so that theoretically expected performance and the practical performance (including stability of the material under load and realistic – harsh conditions) are contrasting. This high number of uncertainties underlines that more tailored screening approaches are of much more practical use, where the screening extends and complements know-how and expertise of researchers who are merely using the computational tools. As for the chemical synthesis a screening approach as presented in section 1.1 enables to perform a computational screening of compounds, profiting from the expertise in physico-chemistry of the team of researchers. The balanced choice of theoretical descriptors including stability and performance issues as well as environmental factors, realizes a more directed computational screening than a brute-force high-throughput screening. A similar conceptual screening approach can be tailored to the material's sector as presented in section 1.2. With the established systematic structure-property relationships that are the outcome of such studies, design of materials is greatly facilitated and costs can be reduced by feeding the data in larger-scale models performing device-level simulation to test new ideas in-silico.

## 2 Simulation methods

Theoretical methods to describe structure and dynamics of materials and chemical compounds on the molecular level encompass classical and quantum mechanics. Molecular dynamics simula-

**Figure 6** Computation of melting points ( $T_m$ ) or glass transition temperatures ( $T_g$ ) of metal organic or organic materials. Reaching high accuracy on complex materials properties in a few days. Abbreviations used in the Figure: Aluminiumtris(8-hydroxyquinolin) ( $Alq_3$ ), Tris(4-carbazoyl-9-ylphenyl)amine (TCTA)



tions are often based on the former where interactions between the particles are parametrized as bonds, angles, dihedral angles as well as non-bonded (Coulomb and van der Waals interactions), denoted as the force field (see for example (Mackerell, 2004; Ponder and Case, 2003)). Quantum mechanics, on the other hand, provides, a universal way to mathematically describe the properties of matter.

The accurate ab-initio methods solving the Schrödinger equation (like coupled cluster or perturbation theory methods or quantum monte carlo simulation), however, are in view of the high computational costs not very frequently used and their application is so far limited to academic show-cases rather than industry-relevant species. A list of recommendable methods and their characteristics are shown in Table 2.

In contrast to the accurate universal bottom-up quantum description, empirical expressions can be used that represent a chemical species by a predefined topology (connectivity). The simulated molecular dynamics using relatively simple potential functions is attractive to predict the structural behavior, especially of soft matter. The low computational costs allowing to simulate rather long

timescales of the dynamics of big systems, with the state of the art being for example a full virus capsid (64 million atoms, 100 ns) (Zhao et al., 2013). The drawback of classical mechanics is its limitation to a single chemical species, so that chemical transformations or other processes with a change in electronic structure can only be incorporated with more complicated extensions such as a reactive force field (Van Duin et al., 2001) or the empirical valence bond method (Kamerlin and Warshel, 2011; Warshel and Weiss, 1980). Furthermore, there exist severe limitations in the systems that are well described by current standard parameter sets, especially regarding transition metals. Addressing this problem, quantum chemistry is of great help. In Grimme's QMDF approach, for example, the usual parametrization of representative building blocks by hand is replaced by a tailored system-dependent QM calculation (Grimme, 2014), which can even be applied to rather complicated transition metal complex-containing systems, and still bear all benefits of a classical potential simulation.

This development already points into future directions, where combinations of universal quantum descriptions together with a suitable param-

**Table 2** Recommendable methods for quantum mechanics-based studies. Abbreviations used in the table: Double hybrid density functional (DH-DFT), high performance computer (HPC).

Type	Accuracy	Speed	Example	Computer	Application
Molecular mechanics	medium to high	very high	QMDF	Notebook to server	Molecular dynamics
Approximate QM methods	low to high	high	PM6-D3H+, OM3-D3, DFTB3	Desktop to server	Molecular dynamics static
DFT	low to high	medium	PBE0-D3BJ, B3LYP-NL, PW6B95-NL, wB97X-V	Server to high end server	Optimization of geometries, computation of energies
DH-DFT	high	low	B2GPPLYP-D3BJ, DSD-PBE-NL, xDH-PBE0, PWPB95, PWRB95	High-end server	Computation of accurate geometries and energies
Coupled cluster	very high	very low	CCSD(T), DPLNO-CCSD(T)	High-end server HPC center	Computation of reference data



etrization to lower the computational costs will be further developed. Incorporation of electron correlation and treating metals will be the challenge for and the advancement of semi-empirical methods exceeding the currently available methods and parametrizations like PM6-D3H+ (Stewart, 2007; Kromann et al., 2014), DFTB3 (Koskinen and Mäkinen, 2009; Gaus et al., 2011).

Intermediate between highly empirically parametrized methods and parameter-free ab-initio quantum chemistry is the density functional theory (DFT) that is the workhorse method in computational chemistry. This method provides high accuracy in many cases on the one hand and manageable computational costs on the other. Because it is impossible to test all available methods regarding the applicability to a given problem, benchmark studies – that is testing a number of methods for a representative class of test-molecules - are often performed to measure their suitability. Although there are a number of benchmarks for a large range of computational tasks, e.g. noncovalent interactions (Burnset et al., 2011) and excited states, it is a well-accepted fact, that there exists no all-purpose method that yields acceptable results throughout all phenomena and all classes of molecules. For example, for quite some time, the B3LYP hybrid functional has been regarded as such all-purpose model chemistry, however, in the recent past, the opposite has been proven (Sure and Grimme, 2015; Kruse et al., 2012; Grimme et al., 2010). Often, this functional provides the worst compromise among comparable methods, while well-chosen state-of-the-art functionals may operate within the experimental uncertainties. Sometimes, DFT itself fails to qualitatively describe the molecule of interest so that, despite the higher computational costs ab-initio approaches have to be chosen.

One direction to overcome inherent errors in the DFT methodology is to use parameters in the functional and to parametrize the method to a given test set. For example, the Mo6 functional employs a number of 36 parameters determined by a large benchmark study (Zhao and Truhlar, 2008). However, past experience suggests that these methods are mainly suited for systems of marked similarity to the ones included in the fitting sets. Benchmarks from arbitrary molecular systems which are not covered by fittings, such as the “Mindless Benchmark” set (Korth and Grimme, 2009), contribute significantly towards the identification of generally applicable methods. Notice that there exists also the alternative strategy: improving the underlying theoretical framework without introducing empirical parameters. The prominent example of this direction bases on the relatively old PBE functional (Perdew et al., 1996)

that has experienced several modifications with a modern functional addressing major drawbacks of DFT (Eshuis and Furche, 2011; Zhang et al., 2012; Adamo and Barone, 1999).

Substantial inherent errors in pure density functional theory include the lack of van der Waals type of interaction that originates from dynamical correlation. Such interactions are conveniently introduced by an atom pair-wise dispersion potential of which the most recent and prominent is Grimme’s D3 correction (Grimme et al., 2011) which requires only minimal additional computational effort. Another description based on the electron density is also available with the VV10 method (Hujó and Grimme, 2011; Vydrov and Van Voorhis, 2010) as -NL extension to existing density functionals, being calculated during the density functional evaluation and of higher computational cost. The inclusion of dispersion interactions has become increasingly important, in particular for the more accurate description of charged molecules or organo-metallic systems, allowing for an appropriate examination of industry-relevant systems such as catalysts or magnetic materials (Grimme et al., 2016).

Other DFT approaches like Meta-GGA (Mo6 (Zhao and Truhlar, 2008), PW6B95 (Zhao and Truhlar, 2005), TPSSo (Tao et al., 2003)) and range separated functionals (CAM-B3LYP (Yanai et al., 2004),  $\omega$ PBEh (Rohrdanz et al., 2009),  $\omega$ B97X (Chai and Head-Gordon, 2008)) lead to an even better description of structural parameters and electronic excited states.

A great leap in the accuracy which exceeds pure DFT functionals was achieved as a result of new methods such as the group of double hybrid functionals. For instance, the prototype B2PLYP-D3 and derivatives (Goerigk and Grimme, 2014) have become state-of-the-art methods for the calculation of very accurate thermodynamic data in an acceptable period of time. Latest developments, such as PWRB95, deliver excellent results which are comparable to the classic double hybrids, while requiring lower computational expenses which range between DFT and DH-DFT. Ab initio methods such as CCSD(T) are frequently regarded as standard reference due to their very high accuracy. As a result of simplifications such as DLPNO-CCSD(T), their high computational cost can be significantly reduced (Riplinger and Neese, 2013; Riplinger et al., 2013). A simplified comparison of computational cost of some popular simulations methods is shown in Table 3.

In conclusion, all above, computational materials or synthesis discovery is far from being a black-box work-flow including subtle challenges in the application of the appropriate theoretical framework. This complexity requires expertise, experi-

**Table 3** Simplified comparison of the relative computational costs of different simulation methods normalized per SCF iteration (Abbreviation used in the table: Lysergic acid diethylamide (LSD); Number of atoms in parentheses).

Computational costs	PM6-D3H+	PBEo-D3	Mo6	$\omega$ B97X-D3	B2-PLYP-D3	CCSD(T)
Benzene (12)	0.0023	1	1.02	1.4	1.8	188
Caffeine (24)	0.0002	1	1.02	1.5	1.8	-
LSD (49)	0.0001	1	1.09	1.5	2.1	-

ence and continuous testing and validation of the predictions, all being best-practice in computational materials or syntheses discovery.

### 3 Conclusion and Outlook

Computational chemistry has become a well-established tool in academic research as well as in industry. The application of quantum mechanics delivers knowledge at the molecular level, particularly on what is happening at specific chemical reaction steps and why certain material properties arise.

Even though there already exists a high number of innovative simulation methods, new simulation methods and potential game-changers are continuously being developed. For instance, if new approaches or significantly more efficient computer technologies can access the world of process-scale molecular dynamics (covering realistic timescales of milliseconds to seconds) by accurate methods that rely on none or only few empirical parameters, new insights into temperature and concentration-dependent effects of chemical reactions or materials may become available for additional areas, such as semiconductors, fuel cells and automotive or IoT (Internet of Things) batteries. On the other hand, new methods with a comparable accuracy like DFT and at the cost of semi empirical methods would also have a massive impact on the size of virtual high throughput screenings and in data generation for innovative machine learning algorithms to develop a specialized artificial intelligence for chemistry.

The modification of chemical systems, the computation of properties and their analysis can be automated in many areas; current virtual high throughput screening technologies allow improvements of chemical synthesis or of a material to be

rapidly identified. This reduces personnel requirements as well as development time and costs significantly, as only the most promising systems need to be analyzed in the laboratory. Consequently, competitors who rely on cheap labour and fewer regulations may lose their competitive advantage because scalable quantum chemical investigations can be done faster, cheaper and analyse more details. With the help of modern, highly accurate simulation methods, enormous productivity gains and faster time-to-market can be achieved.

However, this advancement comes with a cost: the high diversity of suitable and unsuitable methods and approaches renders it often virtually impossible for individual professionals to effectively and competently cover this cross-sectional technology (combining quantum mechanics, chemistry, physics, materials science as well as hardware and software technology). Experience shows that only a multidisciplinary and experienced team of chemists, quantum chemists, physicists and IT specialists is able to produce relevant and realistic simulation data and to process and evaluate it in a very fast way and support the industries R&D specialists with key information at molecular level to develop new game-changing syntheses and materials.

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## References

- Adamo, C., Barone, V. (1999): Toward reliable density functional methods without adjustable parameters: The PBE0 model, *The Journal of Chemical Physics*, **110** (13), pp. 6158-6170.
- Andersson, M. P., Bligaard, T., Kustov, A., Larsen, K. E., Greeley, J., Johannessen, T., Christensen, C. H., Nørskov, J. K. (2006): Toward computational screening in heterogeneous catalysis: Pareto-optimal methanation catalysts, *Journal of Catalysis*, **239** (2), pp. 501-506.
- Burns, L. A., Vázquez-Mayagoitia, Á., Sumpter, B. G., Sherrill, C. D. (2011): Density-functional approaches to noncovalent interactions: A comparison of dispersion corrections (DFT-D), exchange-hole dipole moment (XDM) theory, and specialized functionals, *The Journal of Chemical Physics*, **134** (8), pp. 1-25.
- Chai, J.-D., Head-Gordon, M. (2008): Long-range corrected hybrid density functionals with damped atom-atom dispersion corrections, *Physical Chemistry Chemical Physics*, **10** (44), pp. 6615-6620.
- Curtarolo, S., Hart, G. L. W., Nardelli, M. B., Mingo, N., Sanvito, S., Levy, O. (2013): The high-throughput highway to computational materials design, *Nature Materials*, **12** (3), pp. 191-201.
- Eshuis, H., Furche, F. (2011): A parameter-free density functional that works for noncovalent interactions, *Journal of Physical Chemistry Letters*, **2** (9), pp. 983-989.
- Gaus M., Cui Q., Elstner M. (2011): DFTB3: Extension of the Self-Consistent-Charge Density-Functional Tight-Binding Method (SCC-DFTB), *Journal of Chemical Theory and Computation*, **7** (4), pp. 931-948.
- German Catalysis Society (2010): Roadmap for Catalysis Research in Germany: Catalysis – A key technology for sustainable economic growth, Dechema, Frankfurt.
- Goerigk, L., Grimme, S. (2014): Double-hybrid density functionals, *Wiley Interdisciplinary Reviews: Computational Molecular Science*, **4** (6), pp. 576-600.
- Greeley, J., Jaramillo, T. F., Bonde, J., Chorkendorff, I., Nørskov, J. K. (2006): Computational high-throughput screening of electrocatalytic materials for hydrogen evolution, *Nature Materials*, **5**, pp. 909-913.
- Grimme, S. (2014): A general quantum mechanically derived force field (QMDF) for molecules and condensed phase simulations, *Journal of Chemical Theory and Computation*, **10** (10), pp. 4497-4514.
- Grimme, S., Antony, J., Ehrlich, S. and Krieg, H. (2010): A consistent and accurate ab initio parametrization of density functional dispersion correction (DFT-D) for the 94 elements H-Pu, *The Journal of Chemical Physics*, **132** (15), pp. 1-19.
- Grimme, S., Ehrlich, S., Goerigk, L. (2011): Effect of the damping function in dispersion corrected density functional theory, *Journal of Computational Chemistry*, **32** (7), pp. 1456-1465.
- Hujo, W., Grimme, S. (2011): Performance of the van der Waals density functional VV10 and (hybrid)GGA variants for thermochemistry and noncovalent interactions, *Journal of Chemical Theory and Computation*, **7** (12), pp. 3866-3871.
- Jain, A., Hautier, G., Moore, C. J., Ping Ong, S., Fischer, C. C., Mueller, T., Persson, K. A., Ceder, G. (2011): A high-throughput infrastructure for density functional theory calculations, *Computational Materials Science*, **50** (8), pp. 2295-2310.
- Kamerlin, S. C. L., Warshel, A. (2011): The empirical valence bond model: Theory and applications, *Wiley Interdisciplinary Reviews: Computational Molecular Science*, **1** (1), pp. 30-45.
- Korth, M., Grimme, S. (2009): Mindless DFT benchmarking, *Journal of Chemical Theory and Computation*, **5** (4), pp. 993-1003.
- Koskinen, P., Mäkinen, V. (2009): Density-functional tight-binding for beginners, *Computational Materials Science*, **47** (1), pp. 237-253.
- Kromann, J. C., Christensen, A. S., Steinmann, C., Korth, M., Jensen, J. H. (2014): A third-generation dispersion and third-generation hydrogen bonding corrected PM6 method: PM6-D3H+, *PeerJ*, pp. 1-18.
- Kruse, H., Goerigk, L., Grimme, S. (2012): Why the standard B3LYP/6-31G\* model chemistry should not be used in DFT calculations of molecular thermochemistry: Understanding and correcting the problem, *Journal of Organic Chemistry*, **77** (23), pp. 10824-10834.
- Mackerell, A. D. (2004): Empirical force fields for biological macromolecules: Overview and issues, *Journal of Computational Chemistry*, **25** (13), pp. 1584-1604.
- Maier, W. F., Stowe, K., Sieg, S. (2007): Combinatorial and high-throughput materials science, *Angewandte Chemie: International Edition*, **46** (32), pp. 6016-6067.
- Perdew, J., Burke, K., Ernzerhof, M. (1996): Generalized Gradient Approximation Made Simple, *Physical review letters*, **77** (18), pp. 3865-3868.
- Riplinger, C., Neese, F. (2013): An efficient and near linear scaling pair natural orbital based local coupled cluster method, *Journal of Chemical Physics*, **138** (3), pp. 1-18.
- Riplinger, C., Sandhoefer, B., Hansen, A., Neese, F. (2013): Natural triple excitations in local coupled cluster calculations with pair natural orbitals, *Journal of Chemical Physics*, **139** (13), pp. 1-13.

Rohrdanz, M. A., Martins, K. M., Herbert, J. M. (2009): A long-range-corrected density functional that performs well for both ground-state properties and time-dependent density functional theory excitation energies, including charge-transfer excited states, *Journal of Chemical Physics*, **130** (5), pp. 1-8.

Stewart J. J. P. (2007): Optimization of parameters for semiempirical methods V: Modification of NDDO approximations and application to 70 elements, *Journal of Molecular Modeling*, **13**, pp. 1173-1213.

Stewart, J. J. P. (2013): Optimization of parameters for semiempirical methods VI: more modifications to the NDDO approximations and re-optimization of parameters, *Journal of Molecular Modeling*, **19** (1), pp. 1-32.

Sure, R., Grimme, S. (2015): Comprehensive Benchmark of Association (Free) Energies of Realistic Host-Guest Complexes, *Journal of Chemical Theory and Computation*, **11** (8), pp. 3785-3801.

Tao, J., Perdew, J. P., Staroverov, V. N., Scuseria, G. E. (2003): Climbing the Density Functional Ladder: Non-Empirical Meta-Generalized Gradient Approximation Designed for Molecules and Solids, *Physical Review Letters*, **91** (14), pp. 1-4.

Van Duin, A. C. T., Dasgupta, S., Lorant, F., Goddard, W. A. (2001): ReaxFF: A reactive force field for hydrocarbons, *Journal of Physical Chemistry A*, **105** (41), pp. 9396-9409.

Vydrov, O. A., Van Voorhis, T. (2010): Nonlocal van der Waals density functional: The simpler the better, *Journal of Chemical Physics*, **133** (24), pp. 1-9.

Yanai, T., Tew, D. P., Handy, N. C. (2004): A new hybrid exchange-correlation functional using the Coulomb-attenuating method (CAM-B3LYP), *Chemical Physics Letters*, **393** (1-3), pp. 51-57.

Zhang, I. Y., Su, N. Q., Brémond, É. A. G., Adamo, C., Xu, X. (2012): Doubly hybrid density functional xDH-PBE0 from a parameter-free global hybrid model PBE0, *Journal of Chemical Physics*, **136** (17), p. 1-8.

Zhao, G., Perilla, J. R., Yufenyuy, E. L., Meng, X., Chen, B., Ning, J., Ahn, J., Gronenborn, A. M., Schulten, K., Aiken, C., Zhang, P. (2013): Mature HIV-1 capsid structure by cryo-electron microscopy and all-atom molecular dynamics, *Nature*, **497** (7451), pp. 643-646.

Zhao, Y., Truhlar, D. G. (2005): Design of density functionals that are broadly accurate for thermochemistry, thermochemical kinetics, and nonbonded interactions, *Journal of Physical Chemistry A*, **109** (25), pp. 5656-5667.

Zhao, Y., Truhlar, D. G. (2008): The Mo6 suite of density functionals for main group thermochemistry, thermochemical kinetics, noncovalent interactions, excited states, and transition elements:

two new functionals and systematic testing of four Mo6-class functionals and 12 other functionals, *Theoretical Chemistry Accounts*, **120** (1), pp. 215-241.

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