Postdoctoral Fellowship Junior

Massimo Bocus - 1269725N

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Postdoctoral Fellowship Junior

GENERAL

If granted, this fellowship will start on the following date.

Default start date is October 1. Alternatively, November 1 is also possible.

1 October

Enter the English title of your research proposal.

Chemically-accurate reaction rates for complex, heterogeneous catalytic systems

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Enter the Dutch title of your research proposal.

Chemisch-nauwkeurige reactiesnelheden voor complexe, heterogene katalytische systemen

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Complete the abstract of your research proposal - English version.

Computing accurate rates for reactions occurring in complex environments is very challenging, primarily due to the exponential dependence of kinetic constants on activation enthalpy and entropy. Chemically accurate enthalpies require advanced electronic structure methods, whereas configurational freedom must be taken into account for entropies using dynamic methods such as transition interface sampling (TIS). Combining both was thus far virtually impossible for the prohibitive computational cost. Yet, computing accurate rates is essential not only to explain experimental outcomes, but also to guide and predict them. This project will harness the power of state-of-the-art machine learning potentials (MLPs) to model activated events with chemical accuracy. We focus on zeolite catalysis, but the methods are of general applicability for activated events in complex environments. MLPs will allow us for the first time to combine advanced simulation methods such as TIS and grand canonical Monte Carlo to derive chemically accurate reaction models, first for simple molecular systems and then in well-defined zeolite environments. Finally, all methodological advances will enable to tackle the industrially relevant zeolite-catalyzed direct alcohol amination, conducted under challenging high-loading conditions. The project will be executed in synergy with leading theoretical and experimental partners to validate our models and provide additional insights into the investigated reactions.

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Complete the abstract of your research proposal - Dutch version.

Het berekenen van nauwkeurige reactiesnelheden in complexe omgevingen is uitdagend omdat de kinetische constanten exponentieel afhankelijk zijn van de activeringsenthalpie en de rol van entropie. Voor chemisch accurate enthalpieën zijn geavanceerde elektronische structuurmethoden nodig, terwijl dynamische methoden zoals ‘transition interface sampling’ (TIS) nodig zijn voor entropieën. Het combineren van beide was tot nog toe onmogelijk vanwege de hoge computationele kost. Dit project benut grensverleggende machine learning potentialen (MLPs) om geactiveerde gebeurtenissen chemisch nauwkeurig te modelleren. We focussen op zeolietkatalyse, maar de ontwikkelde methoden zullen algemeen toepasbaar zijn voor reacties in complexe moleculaire omgevingen. MLPs laten toe om geavanceerde bemonsteringsmethoden, zoals TIS en groot kanonische Monte Carlo simulaties te combineren om chemisch accurate reactiekinetiek te bekomen in eerste instantie voor eenvoudige moleculaire systemen en nadien in complexe zeolietomgevingen. Finaal beogen we de behandeling van de industrieel relevante zeoliet-gekatalyseerde directe alcoholaminering, in aanwezigheid van complexe beladingen. Het project zal in synergie worden uitgevoerd met prominente theoretische en experimentele partners ter validatie van de methoden en extra inzichten te bekomen van de onderzochte reacties.

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Enter the English title of your PhD dissertation.

Specify promotor, research group and host institution.

Towards state-of-the-art molecular simulations for an accurate modeling of intricate zeolite-catalyzed reactions; Promotor: Prof. Veronique Van Speybroeck; Research group: Center for Molecular Modeling; Host institution: Ghent University

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Enter the Dutch title of your PhD dissertation.

Naar state-of-the-art moleculaire simulaties voor een nauwkeurige modellering van complexe zeoliet-gekatalyseerde reacties

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Select up to five scientific disciplines that best characterize the proposed research.

Theoretical and computational chemistry not elsewhere classified

Statistical mechanics in chemistry

Computational materials science

Heterogeneous catalysis

Quantum chemistry

Enter up to three English free-text keywords or concepts that best characterize the proposed research.

These keywords allow reviewers to quickly understand the broad scope of your proposal.

reaction kinetics

zeolite catalysis

machine learning potentials

Enter up to three Dutch free-text keywords or concepts that best characterize the proposed research.

These keywords allow reviewers to quickly understand the broad scope of your proposal.

reactiekinetiek

zeolietkatalyse

machine learning potentialen

PERSONAL DATA

This section mainly relates to the evaluation criterion ‘candidate’, your scientific contribution in general, and your motivation and substantiation of relevant competences to carry out postdoc research.

Explain any career breaks.

Make sure your current position and previous appointments are well listed in the e-portal 'Personal details' section ("Posts / Career").
Explain possible 'gaps' in your CV in the input field below. If you have interrupted your academic career at any given point for at least three months (maternity leave, parental leave, full-time sickness leave, 'unconventional' career paths such as leave because of activities in industry or other non-academic sectors, ...) provide details about this below (reason, start/end date). This will allow the reviewers to fairly assess your career stage.

None

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The range of input fields below offer you the opportunity to present a diverse range of career related activities, and of scientific output and achievements, in a context where FWO wishes to leave room for different profiles of academic researchers. That diversity will also be taken into account during the evaluation of your application. The input fields are structured according to the scoring grids, used by the expert panels.

Scientific contribution

List your (up to five) main achievements, including your most important publications.

Here you can mention the publications and/or other achievements within the past 5 years you consider most relevant in order to prove your competences with regard to this fellowship application. The total number of all items (publications and other achievements) taken together amounts to five.
For publications: list all authors, title of publication and journal name (without abbreviations) with volume, start/end page and year. Mention whether the publication was peer reviewed or not. For book publications, give all necessary bibliographic information (author(s) or editor(s), book title, publisher, place, year, number of pages).
Make sure your complete publication list is up to date in the e-portal 'Personal details' section ("Publications").
For other achievements: provide a short description, when it was undertaken and finalised and list all the relevant participants involved in it.

Mind, do mention for each achievement item (publications and other achievements) ***your share*** *and its nature, and those of other significant partners in the workload.*

1. Insight into the effects of confined hydrocarbon species on the lifetime of methanol conversion catalysts
I. Lezcano-Gonzalez*, E. Campbell, A. E. J. Hoffman, M. Bocus, I. V. Sazanovich, M. Towrie, M. Agote-Aran, E. K. Gibson, A. Greenaway, K. De Wispelaere, V. Van Speybroeck* and A. M. Beale*, Nature Materials, 2020, 19, 1081-1087. Peer reviewed. IF: 41.2 [Q1]. Citations‡: 39.
I performed simulations to derive mechanistic insights in MTO deactivation. The project was led by A. Beale's group (UCL). This showcases my proficiency in bridging theory and experiment to enhance process understanding.

2. Shape-selective C–H activation of aromatics to biarylic compounds using molecular palladium in zeolites
J. Vercammen, M. Bocus, S. Neale, A. Bugaev, P. Tomkins, J. Hajek, S. Van Minnebruggen, A. Soldatov, A. Krajnc, G. Mali, V. Van Speybroeck* and D. De Vos*, Nature Catalysis, 2020, 3, 1002-1009. Peer reviewed. IF: 37.8 [Q1]. Citations‡: 32.
I am leading computational author of this collaboration led by D. De Vos' group (KU Leuven), investigating Pd-loaded zeolites for an innovative toluene homocoupling process. My ability of synergistically work with experimental partners was crucial to strengthen our understanding of the process at hand and propose a realistic explanation for the reaction selectivity.

3. Mechanistic Characterization of Zeolite-Catalyzed Aromatic Electrophilic Substitution at Realistic Operating Conditions
M. Bocus, L. Vanduyfhuys, F. De Proft, B. Weckhuysen and V. Van Speybroeck*, JACS Au, 2022, 2, 504-514. Peer reviewed. IF: 8.0 [Q1]. Citations‡: 9.
I spearheaded this theoretical study focusing on the existence of positively-charged arenium ions in hydrated zeolites. This proves my ability of modeling and resolve complex mechanisms in intricate and dynamic environments.

4. Nuclear quantum effects on zeolite proton hopping kinetics explored with machine learning potentials and path integral molecular dynamics
M. Bocus†, R. Goeminne†, A. Lamaire, M. Cools-Ceuppens, T. Verstraelen and V. Van Speybroeck*, Nature Communications, 2023, 14, 1008. Peer reviewed. IF: 16.6 [Q1]. Citations‡: 3.
I initiated the idea of using MLPs to obtain accurate reaction rates with reactive flux including nuclear quantum effects (NQEs). I collaborated with my colleagues R. Goeminne (MLP expertise) and A. Lamaire (NQE expertise). This shows my ability of proposing novel ideas and collaborations to

achieve results beyond individual competences.

5. Operando modeling of zeolite-catalyzed reactions using first-principles molecular dynamics simulations
V. Van Speybroeck*, M. Bocus, P. Cnudde, L. Vanduyfhuys, ACS Catalysis, 2023, 13, 11455-11493.
Peer reviewed. IF: 12.9 [Q1]. Citations‡: 0.
I was the second main contributor to this extensive perspective article, which showcases the extensive experience of our group in the field of operando modeling for zeolite catalysis.

*corresponding author.
‡source: Web of Science.
†shared first authorship.

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Other scientific output and impact.

Here you are offered the opportunity to show any distinct ***research output*** *that does not fit in the bibliographic publication list and that is meaningful in a broad sense for your profile with respect to this fellowship application. It may be constituted by a data base, surveys, a technical diagram, software, objects (maquettes, protoypes…), granted patents, keynote lectures or other lectures at scientific or other meetings, the organisation of such meetings, the organisation of or participation in exhibitions, activities as a scientific evaluator for submitted papers or grant applications and the like, and any other type of activity or output you consider to be relevant. Date the output where appropriate.*
Decribe any scientific or other (societal, economic, …) ***impact*** *beyond publications and obtained research funding.*

5 talks in international conferences, most notably:
- Zeolite-catalyzed benzene ethylation: New mechanistic insights from an old-school reaction class. ACS Spring 2021, Online, 05/04/2021 - 30/04/2021.
- The influence of nuclear quantum effects on proton hopping kinetics in the H-SSZ-13 zeolite through ab initio derived machine learning potentials. The Nederlands Catalysis and Chemistry Conference (NCCC), Noordwijkerhout (The Nederlands), 09/05/2022 - 11/05/2022.
- Towards a realistic modeling of complex zeolite-catalyzed reactions: the case of guaiacol demethylation. International Conference on Theoretical Aspects of Catalysis (ICTAC), Lyon (France), 13/06/2022 - 17/06/2022.

4 poster presentations in international conferences/workshops, most notably:
- Ab initio modeling of the zeolite-catalyzed conversion of alkylphenols into phenol and olefins. EuropaCat 2019, Aachen (Germany), 18/08/2019 - 23/08/2019.
- Mechanistic Insights on the Water-Zeolite Synergy in the Conversion of Biomass-Derived Guaiacol. Water in zeolites workshop, Liblice Castle (Czech Republic), 19/09/2021 - 22/09/2021.

Publication of a paper in The Journal of Physical Chemistry B based on my master's thesis results at the University of Turin (promotor: Prof. Piero Ugliengo).

13 awarded full grants for computing time on the Flemish Tier-1 supercomputer (6 as principal investigator, ~4,000,000 CPU hours each). 2 awarded grants for computing time within the EuroHPC Tier-0 consortium (~8,000,000 CPU hours and ~400,000 GPU hours on LUMI (Finland), ~14,000,000 CPU hours on Meluxina (Luxembourg)).

I have been actively involved in the development and testing of the Thermolib python library for the analysis of enhanced sampling simulations (main developer: Prof. L. Vanduyfhuys) and I have served as alpha-tester during the development of the Psiflow library to manage active learning workflows (main developer: S. Vandenhaute).

Peer reviewer for The Journal of Physical Chemistry C.

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List any scientific awards.

Mention the awarding body, title, date, amount and theme.

Medal for the best master's thesis in Chemistry of the academic year 2017/2018, awarded by the University of Turin.

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Motivation and competences

Write a motivation statement.

Elaborate on your personal motivation, research interests and research vision, as well as on how your scientific background and competences fit with the proposed research project. Provide a clear and substantiated overview of expertise built up and skills already developed, as well as of competences yet to be (further) acquired, related to how you envision the development of your further career.

I vividly remember my first computational chemistry class during my studies at the University of Turin. The sheer idea that we could unravel the mysteries of molecules and materials through a computer utterly fascinated me. I knew that was the path I wanted to follow. I believed - and I still do - that computer simulations offer a gateway to invaluable insights in the nanometers world to support and guide the experiment. I chose to specialize in theoretical and organic chemistry, with the desire to use simulations as a lens to understand the world around us. I completed my Master's thesis under the supervision of prof. Ugliengo, studying the structure of the collagen protein with cutting-edge computational methods.

Bridging theory and experiments, in my opinion, is not a pure academic exercise, but a necessity to reduce the environmental footprints of chemical processes towards a sustainable future. Driven by this conviction and by my enthusiasm for international mobility, I moved to Gent after graduation to start a PhD in prof. Van Speybroeck's group. Her research in complex zeolite-catalyzed reactions at operando conditions was at the perfect intersection between theoretical, organic and industrial chemistry to fulfil my interest. Moreover, I could conduct my research in the dynamic environment that is the Center for Molecular Modeling (CMM). I take pride in what I consider a strength of mine, namely my passion for 'scientific chitchatting' with friends and colleagues, where we informally exchange ideas and research visions. Projects that started as a casual exchange have now found their way into the pages of renowned international journals.

One of the topics I started to explore during my PhD and that I personally find extremely fascinating are machine learning potentials (MLPs). This captivating frontier in computational chemistry is deeply revolutionizing our way of approaching a scientific problem. While traditionally simulations are done with resource-intensive quantum mechanical methods, MLPs offer a paradigm shift by retaining analogous accuracy while increasing speed by many orders of magnitudes. MLPs are what I was looking for, a brand new tool to push computational chemists closer to accurately modeling complex catalytic environments.

My PhD explored only the onset of MLPs applications for complex catalytic reactions. Now, my ambition is to push the boundaries further by harnessing their power to model realistic zeolite-catalyzed reactions. I find myself in the privileged position of working in a multidisciplinary team of scientists and, with the opportunities afforded by this fellowship, I will be able to open up new international collaborations to expand my horizons and strengthen my international network. I will capitalize on this unique position to set myself in the front line for the ongoing societal revolution induced by machine learning techniques, whose integration in everybody's life seems unavoidable.

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List your career building activities.

In this field you can mention a range of activities such as education activities, supervision of bachelor, master and PhD students, institutional responsibilities (governance, administration, ...), membership of scientific organisations and societies. (past as well as planned) active participation in networks, research collaborations (apart from research stays), R&D services provided to third parties, relevant training and the like.

In my path towards becoming an independent researcher, I try to diversify my skills by working not only on my research, but also on teaching and supervision. I am therefore glad to serve as assistant in the exercise sessions of three Ghent University courses: two from the Master's degree in Chemical Engineering ('Chemistry of Industrial Processes' and 'Molecular Modeling of Industrial Processes', since 2020) and one from the Master's degree in Engineering Physics ('Modeling and Engineering of the Nanoscale Materials', since 2022).

During my PhD in Ghent University, I had the pleasure to successfully supervise 2 Master's thesis students from Chemical Engineering and 2 Master's thesis students from Engineering Physics in topics ranging from computational catalysis to the development of theoretical methods for the derivation of reaction rates from enhanced sampling molecular dynamics simulations.

I had fruitful collaborations with the experimental groups of Prof. D. De Vos (KU Leuven) and Prof. A. Beale (UCL), which resulted in high-level publications in Nature Catalysis and Nature Materials. I currently actively collaborate with the experimental groups of Prof. U. Olsbye (UiO), Prof. B. Sels (KU Leuven) and Prof. B. Maes (UAntwerpen), and with the theoretical group of Prof. Juerg Hutter (University of Zurich).

I successfully completed the Doctoral Training Program offered by Ghent University during my PhD. Moreover, for the successful execution of this proposal, I plan to partake (or I have already attended) in the following relevant workshops:
- Introduction to CP2K. 11/03/2019 - 13/03/2019 (Ghent, Belgium).
- Understanding Molecular Simulations. 06/01/2020 - 18/01/2020 (Amsterdam, The Nederlands).
- Water in zeolites workshop. 19/09/2021 - 22/09/2021 (Liblice Castle, Czech Republic).
- Short Symposium "Quantum simulation combined with machine learning for catalysis" within the International Congress on Catalysis. 14/07/2023 - 19/07/2023 (Lyon, France).
- A Time Warp in Digital Chemical Discoveries (eScience Center - Lorentz Competition). 02/09/2024 - 06/09/2024 (Leiden, The Nederlands).

The field of machine learning for molecular simulations is currently in rapid evolution and I will make sure to participate in the most relevant workshop and conferences that will be organized throughout the duration of the Postdoctoral fellowship, in order to maximise dissemination of my work and be an integral part of the community. To be aware of the organized events, I will make use of well-known platforms such as Psi-K or the CECAM website.

Finally, I plan to join the Steering committee of Ghent University Postdoc community to refine my leadership and communication skills. They actively organize events for Postdocs at the university, making it an excellent platform to extend my network outside the boundaries of the faculty of Engineering and Architecture.

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Specify earlier mobility (research stays) in other organizations.

Specify any type of organization in Belgium or abroad, contact person, start/end date, function/activities.

I deeply value international mobility, as understandable from my PhD experience abroad. Unfortunately, with most of the PhD under covid restrictions, it was challenging to organize long-term stays in other groups. Nevertheless, I had the pleasure to visit prof. Juerg Hutter Research Group at the University of Zurich. I was visiting researcher from 25/04/2022 to 6/05/2022. Prof. Hutter is the lead developer of the CP2K quantum chemistry software and I used this chance to learn about the use of advanced electronic structure methods in CP2K (MP2, RPA). The collaboration is still ongoing.

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Specify concrete mobility plans within the FWO fellowship: research stays in another organization (up to 12 months).

Specify any type of organization in Belgium or abroad, contact person, start/end date, function/activities. *See Regulations of the Research Foundation – Flanders governing the Postdoctoral Fellowship art.19§2.*

I consider the inclusion of international mobility in this proposal essential to refine collaborations and learn new skills. Hence, I foresee a long-term research stay (~ 3 months during the first half of 2025) at the Norwegian University of Science and Technology (NTNU), in the group of Prof. Titus van Erp. Prof. van Erp is one of the original developers of replica-exchange transition interface sampling (RETIS) and lead developer of the ∞RETIS library, which I will use to perform RETIS simulations in combination with machine learning potentials (MLPs). Working with Prof. van Erp will be quintessential to improve my theoretical knowledge of the latest advancements in RETIS and to efficiently couple MLPs with ∞RETIS, which are both key aspects of WP1.

Because I aim to obtain chemically-accurate rate constants for zeolite-catalyzed reactions, leveraging top-tier experimental partners is key to validate our results and synergistically improve our knowledge of the system under investigation. To maximise collaboration and open a direct communication channel, I plan 2 short research stays (~2 weeks each) in the groups of our experimental partners. I will visit the group of Prof. Unni Olsbye (University of Oslo) in the first phase of WP2. Her group has leading experience in the measurement of kinetic constants for fundamental reactive events in microporous materials. Therefore, we will collaborate to validate the computational results against measured values. Subsequently, at the beginning of WP3, I will visit the group of Prof. David Flaherty (Georgia Tech). Prof. Flaherty is internationally renowned for his detailed mechanistic studies of intricate zeolite-catalyzed reactions. We will collaborate to apply the methods developed and tested in WP1 and 2 to complex, industrially relevant catalytic cycles.

Prof. van Erp, Prof. Olsbye and Prof. Flaherty have all endorsed this proposal and agreed to host me in their respective groups (see attached letters).

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HOST INSTITUTION - SUPERVISOR

This part of the application form provides info on host institutions and (co-)supervisors of your research. There are 3 levels where data can be filled in.

1. ***As a FWO postdoc researcher, you must be affiliated to a main Flemish host institution*. You must refer to a (main) supervisor in this institution.***

   ** Eligible main host institutions are: Universities in the Flemish Community, the Evangelical Protestant Faculty of Leuven, the Faculty for Protestant Theology in Brussels, the Maritime Academy, the Vlerick Business School, the Antwerp Management School, and the Institute of Tropical Medicine.*

   Select a main Flemish host institution (Art. 3§1 of the FWO regulations) from the pick list, and name a main supervisor. The main supervisor will be invited by FWO to submit a recommendation letter. Co-supervisors will receive a notification by FWO.

   (Optional) You can name a co-supervisor, affiliated to the same main host institution.

2. ***(Optional) In case of a collaboration with a Flemish or Federal scientific institution, where the research is carried out, (Regulations Art 3§1), the co-hosting organization and co-supervisor should be named. It should be mentioned on level 2.***

   Select an organization from the pick list, and name a co-supervisor. If needed you can name another co-supervisor affiliated to this organization.*

   ** If the organization is not mentioned on the pick list, select 'other' and name the organization FWO will consider whether this organization fulfills the requirements to act as a co-hosting institute.*

3. ***(Optional) In case another co-supervisor oversees your project. Mention the organization they are affiliated to, and the corresponding co-supervisor. It should be mentioned on level 3.***

1. Main Flemish host institution

Main Flemish host institution

Ghent University (UGent)

Supervisor

As a FWO postdoctoral fellow, you will report to a (main) supervisor in the main host institution. Apart from overseeing and mentoring your project, the role of the main supervisor in an FWO context is also to approve any adaptation of the project linked to the postdoctoral fellowship after its start, they can be asked to hand in medical attestations in cases of medical leave of the fellow, will be informed about any work accident and will have to approve holiday periods of the fellow. ***The (main) supervisor will be invited by FWO to submit a recommendation statement on the postdoctoral fellowship application.***

In case of collaboration with other research units in the same or other host organizations, co-supervisors should be mentioned. These will receive a notification by FWO. They will not be invited to submit recommendation letters.

Title	*anonymized*
First name	Veronique
Last name	Van Speybroeck
Date of birth *(optional)*	*anonymized*
Current occupation	Full Professor, Head of CMM
Employment rate	*anonymized*
Email	*anonymized*
Research unit	Center for Molecular Modeling

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Street and number	*anonymized*
City	*anonymized*

Co-supervisor(s) ***(optional)***

You may specify one or more co-supervisors.

2. Other host institution(s) – Flemish or federal

If you will carry out your research in another host institution (Flemish or federal) according to Art 3 §1 of the regulations, please click "Add" to select an institution in the drop-down menu. If the institution is not mentioned in the picklist, select 'Other' and name the organization. FWO will consider whether this organization fulfills the requirements to act as a co-hosting institute.

3. Other organization(s)

PROJECT

Project description

Project description

The project description should be structured following the template provided by FWO. The sequence of the different topics should be followed exactly as provided in the original template. The total project outline has a maximum of 10 A4 pages (Font Calibri 11, single line spacing, original template margins ...) herein included all tables, graphs, illustrations, etc.

Attachment [Project description] [FWO_proposal_Massimo_final.pdf] has been added below in the report.

Attachment [Project description] [Letter_MassimoBocus_VanErp.pdf] has been added below in the report.

Attachment [Project description] [Massimo_Bocus_invitation_Olsbye.pdf] has been added below in the report.

Attachment [Project description] [Flaherty - Letter of Support for MB.pdf] has been added below in the report.

Other funding

Have the content of this proposal and at least the main part of the proposed research actions, be it with literally the same text or in a varied form, already been submitted before AND was it funded or is the funding decision still pending (applications that finally did not result in funding should not be mentioned)?

No

Enter any additional remarks and the decision date(s) of pending evaluation(s) mentioned above.

- *You are encouraged to use this field as an opportunity to point out potential overlap, complementarity, added value of current funding applied for or already obtained, ... related to the applications mentioned above.*

- *There can be good reason for applying or already having applied for funding at FWO or elsewhere. It is however important that the panel understands how pending applications for funding or obtained funding mentioned above relate to the current application.*

State 'NA' if not applicable.

NA

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Project positioning and embedding

Explain how this project fits into the research activities of the involved host institution(s).

Eleborate on the positioning and embedding of your project in the research group(s). If the project has already been initiated, please state the progress of your research.

This project, conducted at the Center for Molecular Modeling (CMM, http://molmod.ugent.be), aligns perfectly with the group's interdisciplinary approach at the nexus of physics, chemistry, and materials engineering. The CMM, composed by ~40 researchers, has a long-standing leading role in the operando modeling of nanoporous materials, also evidenced by the 2 ERC grants awarded to its lead, Prof. Van Speybroeck out of 3 awarded to members of the group. This proposal, located at the edge between industrial chemistry, statistical physics and computer science, has a large growing potential in the fertile, multidisciplinary CMM ground. Indeed, the group includes experts in all three fields with whom I do or I will collaborate - in order to leverage everybody's expertise. Moreover, thanks to the international collaborations initiated or consolidated within this project, I aim to bring new methodological advances to the CMM. For instance, I will become leading expert in transition interface sampling by collaborating with Prof. van Erp, an advanced technique with which the CMM has nowadays limited experience.

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Position the project in a national and international context.

Mention specific research collaborations planned in the course of this project, if appropriate, mention larger projects, programmes or networks your proposal may be part of.

Each working package of this project relies on international collaborations with renowned researchers in the field. In particular Prof. Titus van Erp (NTNU, Norway), original developer of transition interface sampling and of the ∞RETIS library, Prof. Unni Olsbye (University of Oslo, Norway), who boasts exceptional expertise in the synthesis and characterization of nanoporous materials and Prof. David Flaherty (Georgia Tech, USA), expert in the study of reaction mechanisms in intricate catalytic environments in zeolites. To maximise our collaborative effort, all partners have agreed to host me in their research groups (see attached letters). Additionally, the project will benefit from the extensive network of Prof. Van Speybroeck with international experts (both theoretical and experimental) in the field of catalysis in nanoporous materials. In particular, we have long standing collaborations with Prof. De Vos and Prof. Sels (KU Leuven), Dr. Boronat (ITQ) and Prof. Gascon (KAUST). On a 2-months base I also partake in meetings between the CMM and the experimental groups of Prof. Olsbye and Prof. Bordiga (University of Turin) to synergistically investigate zeolite-catalyzed reactions.

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Did you take the issues of gender/sex and diversity into account while designing your research plan (e.g. selection of human participants and/or animals in experiments, relevance of research questions and/or results with respect to gender differences, …)?

This issue will be taken into account during evaluation as part of your research methodology and work plan.

No

Justification.

Not applicable

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Did you or will you work with societal actors other than research partners in the whole or parts of the research process (from design of the application up to the execution of the research)?

'Societal actors' consist of all kinds of groups in society (like patients and/or their organizations, other citizens, firms, ...) involved in or connected to the research in one way or another. There is no limitation to what kind of partners in society possibly can be included, nor is involving societal partners an obligation: whether such an involvement could be relevant or not is left to the judgment of the applicants of the research proposal. Take into account, however, that the evaluators may find that collaboration with societal actors is recommendable or even necessary; you may anticipate this by clarifying your position in the designated textbox. Please be aware that this question on societal actors does not concern science communication or valorization.

No

Justification.

Not applicable

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Science communication

Indicate how the results of the proposed research will be communicated to a non-expert audience.

FWO encourages its fellows to disseminate the results of their research widely and valorise them where possible.

My research commitment to openness and accessibility aligns with the FAIR principles. As I did during my PhD, I will share my results with Open Access publications in high-impact international journals and in renowned workshops and conferences. I am passionate about science communication and, therefore, fully committed to disseminate the main findings of this project to a non-expert audience. To this end, I will use a variety of channels (including some with which I am already familiar) including: (1) press releases on our website highlighting high-impact publications, in collaboration with the CMM PR office, and on the Ghent University website (see e.g. https://molmod.ugent.be/news/cmm-nature-catalysis-molecular-palladium-zeolites). (2) National and international news outlets and blogs for the general public. (3) The VSC (Vlaams Supercomputer Centrum) has a dedicated platform to share important research outcomes enabled by the use of their infrastructure (https://www.vscentrum.be/researchshowcase). (4) Through the ACS LiveSlides or similar services. (5). Through popularized presentations within Ghent University, such as during the Postdoc day organized by the postdoc community.

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BENCH FEE

Requested bench fee (per project year).

The bench fee allows you to cover costs for items directly related to your research activities as a FWO fellow, and according to article 6 of the regulation for bench fees. Per default, you are entitled a bench fee of € 4,000 per year. You can apply for a higher fee, up to € 10,000 per project year, with motivation.

Project year

Year 1

Bench fee

€ 4,000.00

Project year

Year 2

Bench fee

€ 4,000.00

Project year

Year 3

Bench fee

€ 4,000.00

PEER REVIEW

Internal peer review

There are 31 thematic panels, ranging over 5 scientific domains, and one specific interdisciplinary panel. More details on these panels and their specific scopes can be found here. You should first select a scientific domain, and then select the thematic panel in that domain that best fits your research project. The Specific Interdisciplinary Panel covers interdisciplinary research that meets the functional definition of interdisciplinarity as adopted by this panel.

Select the scientific domain in which your research is situated, then select the appropriate panel.

wt - Science and Technology

Select the appropriate panel.

W&T4POSTDOC - Chemistry

Motivate your choice of expert panel.

Carefully read the scientific scope of the selected expert panel and motivate why your application fits the scope of this panel - i.e. why this panel has the most appropriate expertise to evaluate your proposal.

In this proposal, we want to advance the state-of-the-art in reaction rates calculations. We will apply our findings to derive new mechanistic details in zeolite-catalyzed reactions due to their importance in both established and developing chemical processes. Nevertheless, the fundamental advances derived by combining the use of accurate machine learning potentials with exact kinetic constant calculations are expected to be valuable for the whole computational chemistry community interested in the characterization of rare events and reaction rate calculations. Because of this, the W&T4 panel is ideally suited to evaluate this proposal. Indeed, their scope includes 'Quantum and computational chemistry', 'Homogeneous and heterogeneous catalysis' and 'Mechanisms, dynamics and kinetics of chemical reactions'. This proposal is precisely at the intersection of these three scopes, as we will use advanced computational methodologies to derive mechanisms and kinetics in heterogeneously-catalyzed systems.

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External peer review

Multidisciplinarity

Do you require an external review from an expert with a different scientific expertise profile than the expertise included in the panel you selected?

No

You may request to exclude up to three experts from the evaluation of your proposal as an external reviewer.
Please list a maximum of 3 experts not suitable as referee ***(optional)***

Suggestions for exclusion need to be motivated.
Please click 'Add' to provide the necessary data about each of these experts.

ETHICS

FWO Ethics Table

The table below lists questions about possible ethical aspects in research proposals. Please go through the main table and tick 'YES' for aspect(s) relevant to your proposal. Then ***answer any related sub-questions by clicking on the appropriate ethical topic*** *that becomes listed under 'Ethical Issues'. You can return to the main table by clicking on 'Ethical issues'.*

If you mark a 'yes' for the question, it follows that:

- ***For the questions marked with *:*** *the applicant is legally or on the basis of institutional regulations obliged to ask for an ethical approval at the competent ethics committee of the host institution. Please do take into account that even when there is no obligation with regard to the research itself, for the publication of the results an approval may still be necessary and that no retroactive ethics committee approvals are provided.*

  *If you have answered questions with an * positively, you must submit an ethics approval request with detailed documentation on e.g. study methodology, procedures, informed consent form, insurance, etc to the ethics committee* ***as soon as your application has been approved for funding.*** *Study-specific procedures cannot begin until this ethics approval has been formally given. Only if the approval relates to a work package planned at a later stage of the project, and if legislation allows, the host institution may decide to authorize the researcher to obtain ethical approval at a later stage, i.e. at the latest before the initiation of the relevant part of the research. Please keep in mind that this delayed application/permission is not possible for all research institutions. Also keep in mind that the ethics advisory procedure can take some time and that therefore you should submit your proposal to the ethics committee well in time.*

- ***For the questions that are not marked:*** *Perhaps no ethics approval may be needed for your research proposal. However, please do take into account that your host research institution might have a stricter policy towards ethics approval for certain research topics and methodology. Furthermore, even when there is no obligation with regard to the research itself, for the publication of the results an ethics approval may still be necessary. At any case, the applicant will have to reflect on those issues and take, if necessary, appropriate measures. If in doubt, it is advised to contact the supporting services of your host institution.*

For more information on each of the ethics issues and how to address them, check the FWO webpage on research ethics and the Guidelines on FWO's ethics checklist.

Ethical issues

Are you using human embryos and/or human embryonic stem cells in your study?

No

Does your research involve human subjects?

No

Do you use human cells and/or tissues in your research?

No

Does your study require the processing of personal data?

No

Does your research involve animal testing?

No

Does your research use genetic resources and/or associated traditional knowledge covered by Access and Benefit Sharing legislation and/or the Nagoya Protocol?

No

Does your research involve international collaboration with non-EU countries?

No

Could your research potentially harm the environment and/or the health and safety of people involved?

No

Could your research have dual-use or military applications?

No

Could your research be misused, compromise security and/or human rights?

No

Does your research involve artificial intelligence?

Yes

Are there any other ethical considerations that need to be taken into account?

No

Artificial intelligence

Does your research involve the development, deployment and/or use of Artificial Intelligence?

Yes

Could the development, deployment and/or use of Artificial Intelligence that is based on your research raise ethical concerns related to human rights, values, decision making, and/or can it cause negative societal or environmental impact?

No

Details on ethically sensitive issues per work package ***(optional)***

Give the number and description of the work packages for which you will submit an application to the relevant ethics committee(s).

I hereby acknowledge that an ethical approval is required for issues marked with an asterisk (*) as far as they apply to my project proposal. I will abide by the applicable regulatory framework, law and institutional policies regarding matters, with or without asterisk (*), that apply to my proposal. If an ethical approval is required, I will ensure to obtain this approval from the competent ethics committee of my host institution, at the latest before starting with the ethically sensitive activities.

Yes

DATA MANAGEMENT PLAN

Data management is an integral part of sound scientific research. It covers the description of data and metadata, their storage and long-term preservation, the designation of responsible persons, the handling of highly sensitive

data, and the open access to and sharing of research data.
The FWO has made data management a key element of its policy for all support channels provided by the FWO. The FWO expects researchers to pay due attention to this dimension before, during and for at least five years after their research.
For background information on data management and the procedures regarding the Data Management Plan (DMP), which FWO expects from its applicants when applying for research funding, please see our website.
Please note that the answers to the questions below and the Data Management Plan should cover the full project, including all (inter-) national partners involved in cross-institutional projects.

Describe the datatypes (surveys, sequences, manuscripts, objects ...) you will collect and/or generate and/or (re)use during your research project.

This research project will generate mainly three data types:
1. Input and output of the simulation packages (Psiflow, ∞RETIS). The most important are the dataset of molecular structures used for MLP training (text files) and the MLP model themselves (binary files), which will be stored and shared according to the protocol below.
2. Bash and python scripts for data generation and analysis, also stored according to the protocol below.
3. Peer-reviewed manuscripts will be available on the publisher website and on the academic bibliography service of Ghent University.

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Specify in which way the following provisions are in place in order to preserve the data during and at least 5 years after the end of the research.

Motivate your answer.

- *Designation of responsible person (If already designated, please fill in his/her name.)*
- *Storage capacity/repository*
    - *during the research*
    - *after the research*

The CMM has a dedicated research data management plan in line with Ghent University requirements. During research, data is stored directly on the university HPC infrastructure. After publication, cleaned-up data is safely stored in project shares maintained by the UGent ICT department. Medium term storage (5+ years, <10 TB) includes input and output files, datasets and analysis script. Long term storage (10+ years, <10 GB) includes all input files required to reproduce the published results. Datasets used to train the MLPs and the MLPs themselves will be made available for the community on public repositories (e.g. Zenodo). Prof. Van Speybroeck can be contacted for long-term storage access.

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What is the reason why you wish to deviate from the principle of preservation of data and of the minimum preservation term of 5 years?

NA

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Are there issues concerning research data indicated in the ethics questionnaire of this application form? Which specific security measures do those data require? *(optional)*

NA

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Which other issues related to the data management are relevant to mention?

An issue related to scripting and programming development is version control, as using different versions of the same code might lead to different results at various stages of the project. We will therefore use public software hosts (e.g. Github) to keep track of these changes and ensure reproducibility. The CMM has already a dedicated Github organization with multiple actively maintained repositories (https://github.com/molmod).

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CONSENT

Declaration by the applicant

General

In completing this application, the applicant confirms that to the best of their knowledge and belief, the information in this application is complete and correct.

The applicant will inform FWO immediately if the intended project cannot be carried out as foreseen or if a major change occurs that may hinder the planned implementation of the project.

The applicant declares that they have read and agree with the FWO regulations that form an integral part of the application documents published on the FWO website and that form the legal basis of the future contract. Furthermore, they take note that the FWO is committed to the principles of the European Charter for Researchers and the Code of Conduct for their Recruitment.

The applicant agrees that the data required for the application and follow-up are electronically stored and used by the FWO. The FWO will use the data provided by the applicant according to the legal requirements of data protection in Belgium, including the use of the anonymized data for statistical purposes and reports. As soon as the FWO has processed your application, you will receive a notification message. The FWO respects the Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC (General Data Protection Regulation) in regards to the processing of your personal data. For more information concerning the privacy policy of the FWO, we redirect you to our website: http://www.fwo.be/en/the-fwo/organisation/processing-personal-data-privacy/.

The applicant agrees that the FWO will forward the full application form including their personal data to, as far as applicable, the members of the FWO expert panels and to experts involved in the evaluation of their proposal in Flanders and abroad (EU and outside EU) and to a partner organization. Any of these receiving parties must declare in advance that they will treat data confidentially and that they will not forward the data or the knowledge gained to anyone nor use it for their own purpose. FWO will take the necessary safety measures to assure this data transfer to the aforementioned organizations or persons will take place in a secure and correct way. More information and details, if available, are published on the FWO website.

Furthermore, the applicant agrees that the following information may be included in lists published by the FWO: title/abstract; full name of the beneficiaries/supervisors; host institution(s); scientific domains/disciplines/key words; start date and end date, allocated funding of the project.

The applicant declares that all information provided in the personal data section of the FWO E-portal is accurate and up-to-date according to the instructions of the respective programme (i.e. only the items in de E-portal that are applicable to the type of support you apply for should be filled out).

The applicant declares that it fully meets the definition of a research and knowledge-dissemination organization' as stated in Framework for State aid for research and development and innovation 2022/ C 414/01 [1].

Research Integrity

The FWO watches over the scientific integrity from the moment research funding is applied for until the execution of the research and the publication of the research results. Therefore, researchers benefiting from FWO support as well as their host institutions, (co-)supervisors and other collaborators involved in FWO research are required to adhere to the scientific integrity at all times.

To this end, elementary rules of behaviour have been laid down in the Ethical Code for scientific research in Belgium and the European Code of Conduct for Research Integrity. Both documents are included in the call for research proposals. The FWO assumes that each researcher has acknowledged these codes from the moment the application is submitted and undertakes to comply with their provisions in all stages of the proposed research. This also applies to their host institutions, (co-)supervisors and collaborators involved in FWO research, for whom the applicant bears partial responsibility.

If there is any doubt about the applicability or implementation of a provision, the host institution and/or the researcher responsible for the project at hand will contact the FWO administration in order to clarify or make concrete arrangements about the relevant provision.

[1] an entity (such as universities or research institutes, technology transfer agencies, innovation intermediaries, research-oriented physical or virtual collaborative entities), irrespective of its legal status (organised under public or private law) or way of financing, whose primary goal is to independently conduct fundamental research, industrial research or experimental development or to widely disseminate the results of such activities by way of teaching, publication or knowledge transfer. Where such entity also pursues economic activities the financing, the costs and the revenues of those economic activities must be accounted for separately. Undertakings that can exert a decisive influence upon such an entity, in the quality of, for example, shareholders or members, may not enjoy preferential access to the results generated by it. (Definition of a 'research and knowledge-dissemination organisation').

I agree

Yes

APPLICATION POSTDOCTORAL FELLOWSHIP (junior/senior)
PROJECT OUTLINE (MAX. 10 pages)

Rationale and positioning with regard to the state-of-the-art

Accurately computing reaction rates is a challenging – yet important – task of computational chemists. Indeed, **reaction rates are directly measurable in experiments and provides a tangible bridge between simulations and reality** when studying activated chemical processes such as thermal or catalytic reactions, polymerization, nucleation, etc. If chemically-accurate rates could be routinely computed for these processes, the predictive power of molecular simulations would then be exploitable not only to explain, but also to guide the experiment. The general theoretical concepts behind reaction rates are of course not new. Already in 1889, Arrhenius noted that the kinetic constant of the reaction, k, depends on temperature T according to the relation[1]

$$k = A\exp(-E_\mathrm{a}/k_\mathrm{B}T)\,. \tag{1}$$

A is the so-called pre-exponential factor (approximately constant over moderate temperature ranges), E_a is the activation energy of the reaction and k_B is Boltzmann's constant. Later on, Eyring and others[2] laid the foundations of transition state theory (TST), which reconciled Arrhenius' equation with the atomistic behavior at the nanoscale. In particular, it was shown that the kinetic constant depends on both the activation enthalpy ($\Delta H^\ddagger$) and entropy ($\Delta S^\ddagger$) of the reaction. For a monomolecular reaction:

$$k = \kappa\frac{k_\mathrm{B}T}{h}\exp\left(-\frac{\Delta H^\ddagger - T\Delta S^\ddagger}{k_\mathrm{B}T}\right). \tag{2}$$

Here, h is Planck's constant and $\kappa \leq 1$ may include tunneling and dynamic recrossing corrections. Crucially, Eyring's equation features both enthalpy and entropy in exponential form, leading to the central challenge addressed in this proposal. **Namely, deviations from the true kinetic constant that span many order of magnitudes must be expected if both the enthalpic and entropic contributions to the activation free energy are not determined with high accuracy** (~±4 $\mathrm{kJ{\cdot}mol^{-1}}$ and ~±20 $\mathrm{J{\cdot}K^{-1}{\cdot}mol^{-1}}$). Enthalpy depends largely on the chosen level of theory (LOT), i.e. the method used to evaluate the potential energy surface (PES) of the system, while entropy on the configurational freedom of the system. Hence, it is not only imperative to accurately evaluate the PES, but also to explore it coherently with the temperature of the system. To achieve this, one can perform molecular dynamics (MD) simulations. In MD, the atomic positions are propagated through time according to Newton's equations of motion, producing a physical trajectory in phase space (the space defined by coordinates and momenta of the particles)[3]. A transition state (TS) is a high-energy ridge on the PES that separates two stable states (reactants and products). When sampling in isothermal conditions, the probability of spontaneously crossing TSs with energies larger than few times $k_\mathrm{B}T$ is virtually zero in the limited timescales of MD simulations, hence the definition of rare events[4]. Throughout the years, advanced methods have been developed to overcome this limitation by focusing the sampling effort on the TS region. Two methods are particularly relevant for this proposal: **enhanced sampling molecular dynamics** (ESMD) and **transition interface sampling** (TIS), which are schematically portrayed in **Figure 1a**, **b**. In ESMD (such as metadynamics or umbrella sampling[5]) a bias is applied to a set of collective variables (CVs) $\boldsymbol{\xi} = [\xi_1, \xi_2, \dots, \xi_N]$ that can describe the reaction in function of (some of) the atomic coordinates in the system. The bias enables effective sampling of the PES high-energy regions and to derive a free energy surface (FESs) $F(\boldsymbol{\xi})$. From there, the kinetic constant of the reaction can be approximated using TST or computed exactly (including barrier recrossing) using the reactive flux (RF) formalism[3-4]. In TIS[6] an ensemble of reactive trajectories is generated with a Monte Carlo procedure. The exact rate constant can be derived from the ensemble statistics. TIS does not require to define a CV nor to bias the system, and can therefore be more robust than ESMD for complex reactive paths.

Despite providing dynamically corrected kinetic constants, RF and TIS are seldomly used because of their prohibitive computational cost when evaluating the PES with quantum mechanical (QM) methods. **This problem is very relevant in heterogeneous catalysis** where – because of its widespread use in industry – a computationally-driven improvement to a catalytic process can result in a remarkable economic and environmental impact. On the one hand, very accurate rates are necessary to build comprehensive kinetic models able to explain and predict experimental outcomes. On the other hand, heterogeneous catalysts at operating conditions often display complex reactive environments that require very large atomistic models to be captured[7]. Most of computational catalysis research today is performed using generalized gradient approximation density functional theory (GGA DFT), which is qualitatively robust and moderately cheap. Unfortunately, it is also known for systematically underestimate reaction barriers (often by tens of $kJ \cdot mol^{-1}$), causing rate constants to be potentially off by several orders of magnitude[8]. More accurate methods, such as Møller-Plesset second-order perturbation theory (MP2) or the random phase approximation (RPA), would be preferred but their high computational cost makes them unsuited to perform the hundreds of thousands PES evaluations needed for RF or TIS.

The focus of this project is on a particular class of heterogeneous catalysts, **zeolites**, which we selected for their wide-ranging industrial and technological applications. Zeolites are microporous, crystalline aluminosilicates with strong Brønsted acid sites (BAS) capable of catalyzing a wide range of reactions. Historically, they are the workhorse of oil refineries for processes such as fluid catalytic cracking, while nowadays they are playing a central role in greener technologies including the methanol-to-olefins (MTO) process and the selective catalytic reduction (SCR) of nitrogen oxides[9]. When approaching rate calculations in zeolites, a further challenge must be considered. Before a reaction can occur, **the reactant must adsorb and diffuse in the material** (**Figure 1c**). The adsorption energy can, at least in part, compensate the activation energy leading to an apparent rate constant, which is normally measured in experiments. Computing accurate adsorption energies can be an insidious task. This is especially true for protic molecules in zeolite, where strong interactions with the BAS result in high local concentrations of adsorbate and (partial) BAS solvation[10]. To simulate this type of adsorption processes, advanced techniques such as grand canonical Monte Carlo (GCMC) would be preferred. However, as for TIS or RF, their computational cost is out of reach for QM methodologies[10b]. **In summary, a tremendous gap exists between the simulations allowed by the hardware/software at our disposal and the methodology/level of theory combination that would make computed rates in complex, heterogeneous catalysts chemically accurate**.

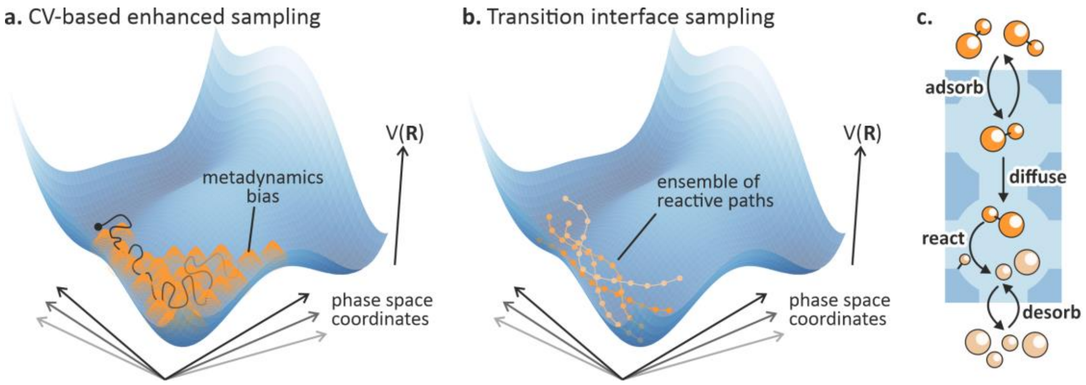

Figure 1. Summary of the two main methods to obtain dynamically correct kinetic constants. The figure illustrates a generic PES (in 2-dimensions for the sake of visualization) explored with ESMD (**a**, the figure is inspired by 2-dimensional metadynamics) and with TIS (**b**). **c.** Schematic depiction of the events occurring during a catalytic reaction in zeolites.

Notwithstanding, we are now entering a new era in computational chemistry driven by the introduction of reliable, data-efficient machine learning potentials (MLPs) [11]. In a nutshell, MLPs are numerical models that accept a collection of atomic coordinates as input and return the total energy and forces of the system. These models can be trained, i.e. optimized to reproduce the energy and forces of a set of structures evaluated with a QM method of desired accuracy. Practically, they become cheap estimators of the QM PES. We showed that for a model zeolite-catalyzed reaction MLPs are about 10^3-10^4 times faster than GGA DFT while retaining analogous accuracy[12]. With an accurate selection of the network hyperparameters and a proper training, the only limit to a MLP accuracy is dictated by the underlying QM method used to generate the training set. More than 15 years after Behler and Parinello's seminal paper about atomic energy predictions with deep neural networks[13], MLPs architectures have largely improved in terms of accuracy and data efficiency. Some of the key innovations that must be mentioned are the use of convolutional neural networks to model the interatomic interactions, the passage from scalar to equivariant tensorial atomic features, and the introduction of higher body-order messages[14]. MLPs can nowadays be trained on a very limited number of structures; so limited that, in fact, generating MP2- or RPA-quality datasets has become a realistic option even for medium to large systems.

In this proposal, we will train accurate MLPs based on advanced first-principles calculations to derive for the first time chemically-accurate rates of intricate zeolite-catalyzed reactions. Given the widespread use of heterogeneous catalysts in existing or emerging industries, the use of machine learning to boost the predictive power of simulations and improve chemical processes is highly coveted. Even big-tech companies are investing in the challenge; a notable example is the Open Catalyst Project from Carnegie Mellon University and Meta AI[15]. Nevertheless, the application of MLPs to catalytic reactions is only recently emerging. We have established proof-of-concept exploration of MLPs to model activated events in zeolite catalysis[12], showing that MLPs can reproduce with high fidelity the PES of the BAS hopping reaction in the H-SSZ-13 zeolite if trained on ESMD simulations. The MLP can be used to perform simulations at multiple temperatures lower than or equal to the training one, compute accurate rates with RF including nuclear quantum effects and also derive kinetic isotope effects. Other groups are also experimenting with MLPs for zeolite-catalysis, examples are the general MLP to model siliceous zeolites proposed by Erlebach et al. and the mechanistic investigations of the SCR process performed by Millan et al. [16] MLPs have not been used thus far to perform accurate TIS simulations, to the best of our knowledge. Only few groups have experimented with fully QM TPS in zeolite catalysis[17]. Because of the prohibitive computational cost, the goal was in all cases to obtain mechanistic insights rather than reaction rates. Yet, TIS can clearly be used to obtain accurate kinetics for non-trivial activated events, such as water autoionization[18]. We believe that the advances in MLP development have led us to a point where applying exact rate calculations to complex catalytic systems has become not only feasible, but the necessary next step to close the gap between simulations and experiment. Hereafter, our proposal for how to tackle this challenging task is outlined.

Scientific research objectives

This proposal aims to employ MLPs trained on high-quality QM data to compute accurate apparent reaction rates based on fully dynamic simulations. We will collaborate closely with experimental partners to compare and validate our findings, with the overarching goal of advancing the predictive capabilities of molecular modeling in heterogeneous catalysis. If successful, the methodology will not only be relevant for the zeolite catalysis community, but will be readily applicable to derive accurate rates for any activated event (nucleation, protein folding, etc.). To reach this ambitious goal, three work packages (WPs) are defined (**Figure 2**):

- **WP1:** We propose an innovative method to actively train an MLP by exploring the PES of rare events with transition path sampling (TPS). With the trained MLP, we will be able to compute accurate rates with TIS. I will have the privilege of being supported by Prof. Titus van Erp (NTNU), who originally proposed TIS and is now lead developer of the ∞`RETIS` library to perform highly-efficient replica exchange TIS[6] (RETIS). Prof. van Erp has agreed to host me in his group for a long-term stay in the first part of this project, to gain expertise with RETIS.

- **WP2:** We will combine advanced simulation methodologies, including the ones developed and tested in WP1, to study well-defined model reactions in zeolites. We will use MLPs to estimate the loading and adsorption energy of the reacting species and derive apparent rate constants. By starting from model reactions, we will be able to leverage our collaboration with Prof. Unni Olsbye (UiO) to compare the simulations results with the experiment. Prof. Olsbye has proven experience in measuring accurate rates for model reactions in zeolites[19].

- **WP3:** We will reach realistic experimental complexity by investigating zeolite-catalyzed reactions with high loadings of protic, reacting molecules to obtain invaluable mechanistic and kinetic insights in environmentally relevant reactions. We will collaborate with Prof. David Flaherty (Georgia Tech) to synergistically investigate the system from both an experimental and theoretical standpoint.

Hereafter, the content of the 3 WPs is outlined with greater detail.

WP1: accurate rate constants from path sampling methods. The latest generation of MLPs has become highly data efficient[14c] thanks to the introduction of equivariant features and higher body-order messages. For instance, for BAS hopping in H-SSZ-13[12] we showed that the number of training structures can be reduced from ~1,000,000 to ~1,000 by introducing equivariant features[18]. These potentials hold the promise to reproduce with high accuracy reference PESs and rates obtained with brute-force QM methods for a negligible fraction of the computational cost. **In this WP, we aim to prove that MLPs can be effectively used to perform RETIS simulations to derive dynamically-corrected reaction rates.** Additionally, we will perform extensive comparison with other methods (RF, TST) to evaluate the respective advantages and disadvantages in terms of accuracy, computational cost, etc. Recently, the open-source `Psiflow` library was developed in our group, the Center for Molecular Modeling (CMM). `Psiflow` implements a variety of active learning algorithms which allow for efficient exploration of the system's phase space without requiring QM MD[20]. The key idea is to let a provisional MLP perform the expensive MD simulations and iteratively improve its quality by extracting structures from the generated trajectories, evaluating them with a QM software and adding them to the training set (**Figure 3a**). To showcase

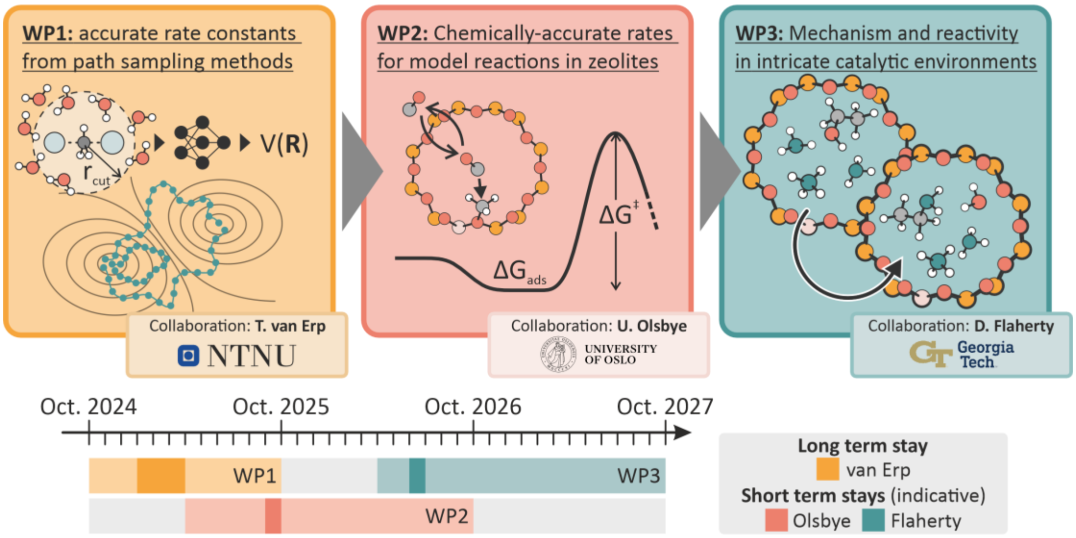

Figure 2. Schematic overview of the WPs foreseen in this proposal with a graphic summary of the investigated reactions and the execution timeline, including research stays in other groups.

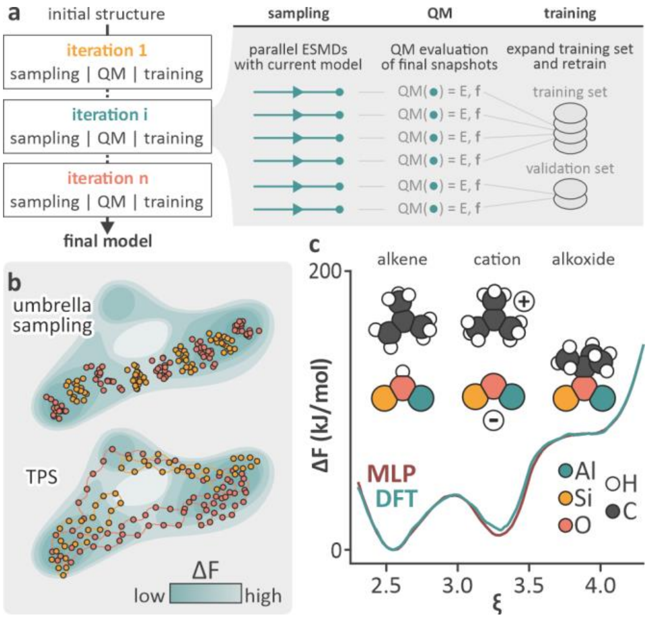

Figure 3. a. Summary of the iterative active learning procedure implemented in `Psiflow`. **b.** Differences in sampling between umbrella sampling and TPS on a fictitious FES. **c.** MLP and DFT free energy profiles for isobutene chemisorption in H-SSZ-13.

its efficiency in modeling complex zeolite-catalyzed reactions, we performed proof-of-concept simulations of isobutene chemisorption in H-SSZ-13. Upon adsorption on the Brønsted acid site (BAS), isobutene can be protonated to form a *tert*-butyl carbenium ion and then bond with the zeolite walls giving a *tert*-butoxide species[21]. We trained a MACE model[14c] based on PBE-D3/TZVP QM evaluations. Phase space exploration was based on umbrella sampling with 100 independent walkers for 25 cycles, giving a total of ~2500 training + validation structures. The final MLP free energy profile for the chemisorption agrees perfectly with the one obtained with brute-force DFT (**Figure 3c**). It must be noted that, from start to finish, generating the MLP profile took about 3 days while the brute force DFT simulations had to run for about 20 days. Moreover, the trained MLP can now be used to perform a large set of additional simulations, as we highlighted in our investigation of the BAS hopping reaction in H-SSZ-13[12]. Presently, `Psiflow` only supports CV-based ESMD to effectively explore the phase space of reactive events. However, the unbiased nature of RETIS could lead the MLP to explore regions of phase space not captured during active learning by the user-defined CV (**Figure 3b**). Moreover, even trial paths that explore high energy regions of the PES must be reliably sampled to either accept or reject them. **We will therefore develop a new type of active learning scheme based on TPS phase space exploration to train an MLP suited for RETIS simulations.** The scheme will be used to train highly accurate, reaction-specific MLPs with analogous accuracy as the underlying QM data.

We will benchmark the MLP-RETIS performances against proof-of-concept chemical reactions with well-known experimental kinetics. We will begin by gas-phase S_N2 reactions with simple molecules (**Figure 4a**). Despite being seemingly trivial, doubts still exist about the actual atomic dynamics in the reaction channel, which would benefit from the mechanistic insights RETIS can provide[22]. Subsequently, we will increase the complexity of the system on two axis: along the first, we will keep the reaction simple (i.e. S_N2) but increase the environment complexity by moving from gas- to solvated conditions. Solvent dynamics and polarity have been indicated to be relevant for the reaction mechanism[23]. Along the second, we will keep the environment simple (gas-phase) but increase the reaction complexity. We will study aromatic electrophilic substitution (S_EAr, **Figure 4a**) as good experimental kinetics data is available while, also in this case, the mechanism is still under debate, in particular concerning the formation of Wheland-type arenium ion intermediates[24]. For this reaction I will benefit from the collaboration between the CMM and the group of Prof. Frank de Proft (VUB), which focused on S_EAr and in which I was actively involved[25]. Finally, we will move to the most complex case-study of WP1, i.e. S_EAr reactions performed in explicit solvent. **This will provide novel mechanistic insights in fundamental classes of organic chemistry reactions that only fully dynamic and unbiased techniques such as RETIS can achieve.**

WP2: Chemically-accurate rates for model reaction in zeolites While WP1 focusses on the intrinsic kinetics and mechanism of chemical reactions, WP2 is devoted to the study of well-defined zeolite-catalyzed model reaction. The main difference with gas- and homogeneous-phase reactions is the necessity of accounting for the adsorption of the gas-phase reactant in the microporous catalyst (**Figure 1c**) to obtain rates that are comparable with the experiment. In current literature, adsorption is often investigated using static simulations with harmonic corrections. It is however well-known that adsorption in zeolites is strongly affected by anharmonic motions, which require dynamic simulations to be properly captured[26]. Ideally, one would perform simulations in the grand canonical ensemble to not only derive accurate heats of adsorption, but also realistic loadings in the material. Unfortunately, advanced simulation techniques such as grand canonical Monte Carlo (GCMC) are too expensive to be combined with a fully QM PES, as converged results may easily require 10^5-10^6 evaluations. Also in this case, we will resort to the exceptional speedup offered by MLPs to unlock QM-quality GCMC simulations in zeolites.

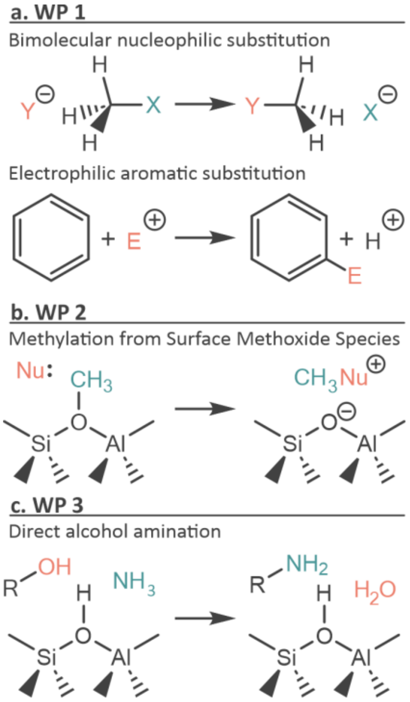

Figure 4. Summary of the reactions investigated in this proposal.

In WP2, we will derive chemically accurate apparent rate constants for well-defined reactive events in zeolites, including the actual reaction and the adsorption step. Recently, a protocol based on MLPs was propose in the CMM to derive QM-quality adsorption isotherms of CO_2 in MOFs (metal-organic frameworks) [27]. We will build on these findings and extend them to zeolite-catalyzed reactions. The actual reactive step will be modeled with the techniques developed and tested in WP1. To validate the unexplored combination of advanced simulations for both the adsorption and reactive steps, we have identified together with our experimental partners from Prof. Olsbye's group a set of reactions that have not only academic and industrially relevance, but also possess 3 key features to facilitate experiment/theory comparison. These features are: (1) there must only be one mobile reacting species to streamline the GCMC simulations, (2) such reactant must also be small to prevent slow diffusion and (3) the reaction must occur on well-defined local active sites. Based on these criteria and Prof. Olsbye's experience, we have selected the methylation of small molecules from surface methoxide species (SMSs, **Figure 4b**) as case study. Methylation events are central to the methanol-to-olefins (MTO) process for carbon incorporation; they occur continuously both in the induction phase, associated with the formation of the first C-C bonds, as well as in the autocatalytic phase, where hydrocarbon pool species are methylated to then expel the reaction products via cracking and dealkylation[9b,28]. Prof. Olsbye's group has recently reported a thorough investigation of small olefins methylation with SMSs using temporal analysis of products (TAP) measurements[19a]. During a TAP experiment, short pulses of reacting molecules are sent to the catalyst at very low pressure and the product stream is investigated via mass spectrometry. The technique can provide a wide range of information about the reaction, including adsorption energies and rate constants. Additional experimental results will be generated for small molecules of interest, in particular CO. CO methylation produces ketene, which is recognized as important intermediate in the induction process of the MTO process and in the CO_2 to hydrocarbon process[29]. **WP2 will stride to bridge the gap between experimental and theoretical kinetics by using advanced simulations techniques based on accurate MLPs. The developed protocol should be of great interest for the computational heterogeneous catalysis community.**

WP3: Mechanism and reactivity in intricate catalytic environments. In this last WP, we will drastically increase the level of complexity by moving toward reactive environments with high loading of co-adsorbed protic molecules. These conditions are omnipresent in modern zeolite-catalysis, where the switch from fossil feedstocks to bio-based ones is associated with the presence oxygenated reacting species (e.g. alcohols). The characterization of zeolite-catalyzed reactions conducted at high loadings of protic molecules is outstandingly challenging from both a theoretical and experimental standpoint. **Hence, their thorough investigation using advanced simulation techniques is the final high-gain goal of this proposal. To this end, we will closely collaborate with the group of Prof. D. Flaherty (Georgia Tech).** Prof. Flaherty is internationally renowned for his detailed experimental mechanistic studies in zeolites, where advanced analysis of the results is used to disentangle contributions to the activation free energy coming from co-adsorbed molecules, steric hindrance, etc. [30] Indeed, complex interactions arise from the coupling between the fast dynamic crossing of the reaction barrier and the slower reorganization of the molecular environment, which makes them an ideal case study for TPS-based techniques and MD simulations.

Motivated by discussions with Prof. Flaherty, we decided to join efforts in investigating the Brønsted-catalyzed direct amination of aliphatic alcohols (**Figure 4c**). This reaction is of great economic and environmental interest. Indeed, it allows to produce useful platform chemicals for the synthesis of polymers and biologically-active molecules starting from bio-derived alcohols[31]. The reaction is mildly exergonic and provides a greener alternative with respect to processes using alkenes (endergonic) or epoxides (toxic). In spite of this high potential, mechanistic studies are limited due to the complexity of the reactive environment[32]. The strong interaction between the reactive partners and the BAS allows to postulate an easy condensation of ammonia within the pores, making the reactive environment more similar to a liquid-solid than a gas-solid reaction.

We will capture the complexity of the reactive environment starting by MLP-powered co-adsorption studies of the reacting molecules (which are made challenging by the reactive nature of the BAS-adsorbate interaction). We will be able to report for the first time accurate isosteric heat of adsorption from grand canonical simulations of reacting adsorbent mixtures. The results will be compared with calorimetric studies performed by Prof. Flaherty's group. Second, we will systematically investigate the reaction mechanism by varying the zeolite topology and the aliphatic alcohol. To this end, we will generate a transferable MLP able to capture the chemistry of the reactive system and use it to obtain mechanistic insights and reaction rates from RETIS and/or RF simulations. Excess free energies caused by the reorganization of the solvating molecules will be extracted from the simulations and compared with the experiment. Finally, all steps will be joined to obtain for the first time a complete, chemically accurate microkinetic model of the reaction in the various catalytic environments. **Thanks to the experimental-computational synergy, we will strive to show that simulations have really reached a point where they can start to accurately predict experimental outcomes even for highly challenging catalytic environments.** While being high-risk high-gain, the overall results of WP3 have the potential to drastically enhance the predictive power of simulations well beyond zeolite-catalysis.

Research methodology and work plan

The successful execution of this proposal does not only rely on known methodology. Instead, a series of new simulation protocols will be developed within the framework of this fellowship. First, we will devise an active learning scheme to generate MLPs suited for path sampling simulations (M1). Second, we will tackle multi-component GCMC simulations of reactive adsorbates (M2). Finally, we will perform kinetic modeling to obtain overall reaction rates of zeolite-catalyzed reactions (M3).

M1: MLP-based path sampling simulations (WP1, WP2, WP3). MLPs are a relatively recent addition to computational chemistry. Nevertheless, we have extensively tested and used them within the

CMM in the past few years[12,20a,27,33]. Therefore, I will consider the choice of the MLP architecture, its training and deployment as consolidated procedures. As mentioned before, `Psiflow` is a new software package recently developed at the CMM which allows to easily and efficiently train MLPs for reactive events (**Figure 3a**). Considering the limited number of QM structures required to accurately learn the PES of this non-trivial reaction (2500 for isobutene chemisorption, see **Figure 3c**), it will be possible to repeat the active learning cycle with a largely improved level of theory, such as MP2 or RPA. During my PhD, I had the opportunity to visit the group of Prof. Hutter in the University of Zurich. Prof. Hutter is lead developer of CP2K and I used the opportunity to become familiar with high-level electronic structure methods such as MP2, RPA and double-hybrid DFT functionals, which have highly efficient implementations in CP2K[34] and can counteract the deficiencies of GGA DFT when modeling (for instance) the chemisorption of unsaturated hydrocarbons in zeolites[8].

We will use chemically accurate MLPs to perform for the first time replica-exchange transition interface sampling (RETIS) simulations and derive kinetic and mechanistic insights in complex reactive events. Thus far, the use of RETIS was limited to very specific reactive events due to the high computational cost[18,35]. We will work with Prof. van Erp, original developer of RETIS, as his group has recently implemented the latest advances in terms of replica exchange and path generation in a new software package, `∞RETIS`[36]. `∞RETIS` uses a combination of infinite rate replica exchange and wire fencing moves to maximize computational efficiency and minimize the chance of path rejection. Its high efficiency, if successfully coupled with the reduced computational cost of MLPs, will allow to obtain very accurate rates and mechanistic details in a matter of hours. MLPs are efficient interpolators but can produce poor results if asked to extrapolate. In practice, this means that the quality of the results can dramatically degrade if the system in exam enters a region of phase space that was not included in the training set. `Psiflow` bases phase space exploration on ESMD and, therefore, the MLPs that can be trained at the moment are not expected to be readily usable for a transition path sampling (TPS) simulation. Indeed, unbiased reactive paths might explore regions of phase space that are not captured by the user-defined collective variable driving the ESMD simulations (**Figure 3b**). For this reason, we will begin WP1 by implementing in `Psiflow` a new active learning scheme based on TPS. The idea is to begin from a limited number of active learning cycles based on metadynamics. This will sample the stable basins (reactant and product) while also generating few reactive trajectories between them. These trajectories are then used as starting point for the TPS-based active learning. In each parallel walker, a new path is generated with standard TPS moves, such as shooting. If the new path still connects reactants and products it is accepted and used as new starting point, otherwise it is rejected. **Remark that both accepted and rejected paths will be included in the training set**, as also the latter have to be learned in order to be reliably rejected in subsequent RETIS simulations. This will make the procedure highly data efficient. After a certain number of TPS moves, the model is retrained based on structures extracted from the accumulated trajectories and the active learning cycle is restarted.

<u>Risks and mitigation:</u> ***The TPS-based active learning does not provide good coverage of the reaction path* (low risk).** More advanced TPS moves can be used to improve the decorrelation between subsequent trajectories, such as wire fencing used in `∞RETIS`. This would make the implementation somehow more complicated but certainly feasible. ***The memory requirements of RPA/MP2 simulations for large periodic systems are excessive* (medium risk).** Cluster-based learning can be used as alternative. There, the energy output of the network is corrected with high-level simulations performed on atomistic clusters of limited size extracted from the periodic model. QM:QM cluster-based corrections are very well-known for zeolite catalysis[21,37] and Tkachenko's group has shown the effectiveness of the approach when simulating whole proteins with a MLP trained on fragment evaluated at hybrid DFT accuracy[38]. Hence, we have strong evidences to support this approach if fully periodic high-level calculations would be unfeasible.

M2: adsorption energies and coverages at operando conditions (WP2, WP3). To derive apparent kinetic constants for zeolite-catalyzed reactions it is quintessential to have good estimates of both the intrinsic rate constant and of the adsorption free energy. We will reliably compute the latter from GCMC simulations. We will build upon the proof-of-concept study recently performed within the CMM, where CO_2 adsorption in MOFs was investigated with MLP-based GCMC[27]. In WP2 we will consider a single adsorbate. We will start by generating structures with multiple loadings by randomly inserting CO molecules in the zeolite framework, using a simple distance criteria to exclude unphysical structures. It is very important that the first active learning iteration includes high-energy structures, as these might be sampled in GCMC and must be reliably rejected[27]. After reaching the desired accuracy, the MLP can be used to perform the GCMC simulations. GCMC itself is a consolidated technique for which many efficient algorithms exist[3].

In WP3, we will probe the adsorption of ammonia/alcohol mixtures at high pressures. This will require the development of a new simulation protocol which combines advanced simulation techniques. First, instead of a single adsorbate we will have to consider a mixture of two adsorbates, both protic and both with a high proton affinity. While simulations from multicomponent mixture in zeolites are known[39], they have not been applied yet to systems in which the interaction between the adsorbate and the active site is so strong. This interaction also causes a second, major issue. It is well-known that high loadings of protic molecules lead to spontaneous solvation of the BAS[10a]. This will inevitably be the case for our system, in which the formation of ammonium ($NH_3 + HZeo \rightarrow NH_4^+ + Zeo^-$) and alkyloxonium ions ($ROH + HZeo \rightarrow ROH_2^+ + Zeo^-$) is virtually sure. This will also cause protons to easily exchange between the protic molecules. It is therefore impossible to define *a priori* the adsorbates identities (intended as list of atomic indices), but they will have to be identified at every GCMC move. We will use geometric criteria to attribute the H atoms in the system to the closest Brønsted base, avoiding deletion moves that would remove positively-charged species (as they would be associated with extremely high energy). In this way, we are confident that we will be able to compute for the first time highly accurate loadings for mixtures of protic molecules in Brønsted acidic zeolites. This is essential to obtain a complete picture of the catalytic processes investigated in WP3, as the solvent organization in the micropores is expected to have a major role on the reaction mechanism and kinetics.

Risks and mitigation: ***GCMC does not converge with protic adsorbates*** **(high risk).** Since protic molecules can condense on the BAS and solvate it, it is possible that sampling the process with simple GCMC will be highly inefficient, hampering convergence. In this case, we will resort to transition matrix Monte Carlo[40] (TMMC). There, a set of regular MD simulations is performed for all loadings of interest and then a transition probability matrix is built with virtual insertion/deletion moves. The advantage is that all loading are included a priori and BAS solvation is automatically sampled in the MD simulations but the technique is relatively more expensive.

M3: reaction rates for complex reactive networks (WP3). In addition to performing advanced reaction rate and adsorption simulations to explore the mechanism and reactivity of the reactions discussed in WP3, we aim to obtain temporal evolutions of products formation at the macroscale to really bridge theory and experiment. This is an ambitious goal, that will require to combine all the microscopical information obtained from GCMC and RETIS in a general microkinetic model for the reaction under investigation. There exist only few examples of microkinetic modeling based on QM simulations in zeolite catalysis[41]. Applying it to systems involving multilayer coverages of reactants mixtures (as in WP3) is far from trivial. We will have to identify general thermodynamic reference states to 'align' the results of the GCMC and RETIS simulations, potentially also including explicitly diffusion in the micropores as they become filled with reactive clusters and less accessible for the reactive molecules. This will give us a set of kinetic differential equations that will be solved using available techniques in literature[42]. The model will provide us with valuable details on the most abundant reactive intermediates and the relative importance of reactive paths, which can complement and explain the experimental measurements.

<u>Risks and mitigation:</u> ***The system of equations in the microkinetic model is too complex to be solved* (high risk).** We can resort to alternative methods to model complex network of reactive events, such as kinetic Monte Carlo. There, stochastic trajectories are explicitly generated by propagating the system from state to state in accordance with the respective kinetic constant.

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November 28, 2023

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Subject: **FWO Postdoc Massimo Bocus**
Letter of invitation from Prof. Titus van Erp (Norwegian University of Science and Technology - NTNU)

Dear Madam, Sir,

With this letter, I wish to express my strong interest to host dr. Massimo Bocus for a research stay within my group in the Department of Chemistry at the Norwegian University of Science and Technology (NTNU), where I am full professor in Theoretical Chemistry. My research focuses on the simulation of rare events and it aims to bring forward the molecular understanding of complex biological and industrial processes using state-of-the-art simulation techniques. We develop innovative computational methodologies to enhance the accuracy of present methods and expand accessible time- and system scales of computer simulations.

We aim to understand processes like chemical reactions, crystallisation, DNA dynamics, adsorption, enzymatic reactions, coalescence, ion transport, and many more. Different to most theoretical and computational chemistry groups in the world is that we focus on the actual dynamics of the molecular processes for which we develop special algorithmic approaches called path sampling. With these techniques, we can calculate reaction rates and analyse reaction pathways which is impossible for standard molecular dynamics as this approach would require centuries of computer time. A central overarching project in our group is the development of our open-source computer code PyRETIS in which we are implementing our simulations methods.

I am highly interested in the topic of the proposal, where the candidate wishes to use machine learning potentials to make a leap forward in the complexity of the systems that can be tackled by PyRETIS. The results of this study will be of great importance to showcase the applicability of path sampling techniques to intricate catalytic systems evaluated with first-principles accuracy.

To support the models developed by the candidate I am glad to host the candidate in my research group for a period of at least 3 months. In this way, we will be able to work together and achieve the best possible coupling between MLPs training/deployment and PyRETIS. I am following the research performed within the Center for Molecular Modeling, already for a long period. I was guest professor from May 2017 till September 2019 at the CMM and some of my researchers have also spent time in Gent. The group of Prof. Van Speybroeck is renowned for her contributions in simulating complex reactions in nanoporous frameworks under operando conditions. The further development of the path sampling method for complex zeolite catalyzed reactions is highly interesting.

The project is very ambitious but I am confident that the targeted goals will be achieved as Massimo has the right background, a proven research track record in related fields, and excellent experience in molecular modelling techniques. This research project will give him the best circumstances to apply path sampling based methods to relevant catalytic reactions, potentially deriving mechanistic insights and quantitative results of unprecedented quality. To ensure cohesion between our groups in this collaboration, and supplement his expertise in reaction modeling with our expertise in path sampling, it is my pleasure to invite Massimo for a research stay of about 3 months in my group. We will support him in implementing the path sampling method in combination with the machine learning potentials. This will also be a central topic in an upcoming workshop “A Time Warp in Digital Chemical Discoveries” of which I am part of the scientific organizers, hosted by the Lorentz Center in The Nederlands. I am confident that high level scientific research results will follow from the collaboration.

Sincerely yours,

T. Erp

Titus van Erp

UiO **Department of Chemistry**
Faculty of Mathematics and Natural Sciences

To whom it may concern

Date: 28 November 2023

Letter of invitation for FWO postdoc Massimo Bocus

With this letter, I would like to support the FWO postdoctoral fellowship of Massimo Bocus. I have a very sustainable collaboration with the group of Prof. Van Speybroeck for many years. Since about two years we are organizing joint group meetings approximately every two months with researchers from my group and the group in Gent, also involving the group of Prof. Bordiga (University of Torino). Within the framework of these online meetings, I got to know Massimo Bocus and got impressed by his in-depth scientific knowledge and research skills. For his postdoctoral application he aims to develop a theoretical framework to determine with high accuracy kinetic rate constants for reactions in zeolites. For this he will use state-of-the-art machine learning potentials (MLPs) in combination with path sampling methods. My group had a tradition in measuring with high accuracy kinetic rate constants of single events in zeolite catalysis. It has shown a tremendous challenge both from experimental and theoretical point of view to estimate the kinetics in complex zeolite environments. This project opens the potential to make a major leap forward to obtain chemically accurate reaction rates, which gives this research the potential of a much broader range of applications beyond those envisioned on the short term.

I am pleased to continue my collaboration with the group in Gent and intensify my interactions with Massimo and to assist him with the experimental part of this project. We will perform kinetic measurements for the reactions taken up in WP2 of the proposal using advanced experimental techniques, such as Temporal Analysis of Products (TAP) set-up or standard kinetic measurements, this will allow to validate his modelling results and synergistically improve our knowledge of the system under investigation. With pleasure I invite Massimo for at least one short visit (about two weeks) to our laboratory where we can conduct the needed experiments, besides discussing the findings of his research.

Sincerely,

U. Olsbye

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November 28th, 2023

RE: FWO Postdoc Massimo Bocus, Letter of invitation from Prof. David Flaherty (Georgia Tech)

To whom it may concern,

I write this letter to offer my strongest support for Dr. Massimo Bocus and his FWO Junior Postdoctoral Fellowship application. I extend an open invitation for Massimo to visit my group at the School of Chemical and Biomolecular Engineering located at Georgia Tech. Our research focuses on overlapping topics of catalysis, surface science and materials synthesis. The goal is to determine the mechanisms of individual elementary steps and competing pathways for chemical reactions necessary to pursue the best use of our limited fossil resources and biomass. To unravel complicated networks of reactions, we utilize steady-state kinetic measurements, transient and perturbation techniques, and *in situ* spectroscopy. With detailed knowledge of how a reaction proceeds we can better design processes and catalysts to selectively promote desirable reactions over the undesirable pathways.

I have followed the theoretical studies of the group of Van Speybroeck for several years. Recently (August 2023), we had the opportunity to exchange research ideas at the Gordon Research Conference - Expanding the Horizons of Porous Materials Design and Applications, which we both attended. I am convinced that a strong synergy could be established between the detailed experimental measurements we perform in my group and *operando* simulations performed in the group of Prof. Van Speybroeck, which would allow to obtain a detailed understanding of the factors contributing the overall reactivity in complex zeolite environments.

Massimo's proposal connects directly with my research interests and on-going projects within my group. Massimo wishes to push borders in the modeling of zeolite catalysis by harnessing the power of state-of-the-art machine learning potentials to better understand and predict complex catalytic systems. We will work together to unravel the mechanism and reactivity of zeolite-catalyzed direct alcohol amination. This reaction is postulated to proceed with very high densities of molecules within the zeolite pores (approximating the density of liquids) given their strong interaction with the pore walls of the zeolite. Within our group, we will use experimental methodologies to quantify the effect of guest species reorganization and confinement on the observed kinetics. I believe these detailed studies will be ideally suited to join forces with the planned theoretical work in Massimo's proposal.

In conclusion, I wish to express my full support for Massimo's FWO Postdoctoral Fellowship application. I look forward to hosting him for a short-term research stay in my group in case his application is granted. Given his proven track record in the modeling of zeolite catalysis and current position within Prof. Van Speybroeck's group, I am confident that Massimo is the ideal candidate for this fellowship and will be highly successful within our collaborative effort.

Sincerely,

Prof. David Flaherty