Chatbot-Assisted Quantum Chemistry for Explicitly Solvated Molecules

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Abstract: Advanced computational chemistry software packages have transformed chemical research by leveraging quantum chemistry and molecular simulations. Despite their capabilities, the intricate design and requirement for specialized computing hardware hinder their applications in the broad chemistry community. Here, we introduce AutoSolvateWeb, a chatbot-assisted computational platform that addresses both challenges simultaneously. This platform employs a user-friendly chatbot interface to guide non-experts through a multistep procedure involving various computational packages, enabling them to configure and execute complex quantum mechanical/molecular mechanical (QM/MM) simulations of explicitly solvated molecules. Moreover, this platform operates on cloud infrastructure, allowing researchers to run simulations without prerequisite computing hardware. As a proof of concept, AutoSolvateWeb demonstrates that combining virtual agents with cloud computing can democratize access to sophisticated computational research tools.

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Computational chemistry has significantly advanced chemistry research in recent decades, from revealing reaction mechanisms[1,2] and interpreting spectroscopy[3-5] to generating training sets for artificial intelligence (AI) assisted design and discovery.[6-8] Advances in theoretical methods and software empower researchers to tackle increasingly complex problems, yet learning to use these tools properly becomes increasingly difficult. Computational chemistry packages, whether for electronic structure calculations or molecular simulations, invariably demand the users' familiarity with the underlying theories and package-specific options, alongside sufficient computing resources for executing them. Many chemical processes necessitate the synergistic usage of multiple packages, posing additional challenges for researchers across the broad chemical science community.

The past decades have seen a growing trend of developing open-source, automated workflows to address this issue. Quantum mechanical (QM) calculation workflows, such as Aflow[9], Material projects,[10] QCDB,[11] and MolSimplify,[12] have significantly enhanced data generation efficiency and software interoperability for data-driven research on solid-state materials and molecules. In addition, AutoSolvate toolkit[13] has streamlined the modeling of explicitly solvated molecules by synergizing QM calculations, force field fitting, and molecular dynamics (MD) simulations, allowing efficient computational investigations of real-life solution phase chemical processes.

However, two major challenges remain. Firstly, crucial simulation parameters must still be set manually, forcing the users to delve into lengthy user manuals. Secondly, the workflows frequently demand appropriate high-performance computing resources, often inaccessible to non-computational researchers. These barriers make the workflows unfriendly to students and experimental chemists. Hence, a more user-friendly computation platform with minimal

knowledge and hardware prerequisites is essential for expanding access to computational chemistry within the broader community.

Here, we introduce AutoSolvateWeb, a chatbot-interfaced, cloud-based computational platform for quantum chemistry studies of explicitly solved molecules, as a proof of concept to address the challenges concurrently. Having achieved automation through the AutoSolvate workflow, AutoSolvateWeb further addresses the accessibility challenge by integrating a chatbot using the Google Dialogflow CX framework. The chatbot educates users through natural language conversations, guides users to configure parameters for modeling explicitly solvated molecules, triggers calculations in the backend, and retrieves the results after completion. In addition, AutosolvateWeb fulfills hardware requirements by conducting all calculations on accessible cloud-computing resources, providing convenient access for anyone with an internet-accessible device.

This work innovatively employs a chatbot to assist users of scientific software, potentially reshaping how scientists interact with advanced research tools. AI chatbot frameworks such as Google Dialogflow, Microsoft Azure Bot service, and Amazon Lex find extensive applications in creating virtual assistants for commercial usages, such as online banking[14] and customer service.[15] Despite their success in other domains, very few AI applications are dedicated to enhancing the user experience of scientific research tools.[16-18] Exceptions include ChemVox[19] for voice-controlled fixed-type quantum chemistry calculations and Coscientist[20] for GPT-4 assisted autonomous chemical experiments. Most scientific software users rely heavily on manuals and expert guidance for multi-step calculations. Through the chatbot integration, AutoSolvateWeb enables non-expert users to perform multi-step simulations of explicitly solvated molecules for the first time without external aids. This convenience empowers researchers from the broad

community to efficiently utilize complex functionalities of scientific computing tools, which marks a significant step forward in integrating AI into scientific research.

Results

Figure 1 illustrates the architecture of AutoSolvateWeb, composed of four containerized services: the AutoSolvate server, the Node server, the Nginx server, and the chatbot server, orchestrated via Docker, an open-source containerization platform. The backend AutoSolvate server, running on CPU/GPU instances on the JetStream2[21] cloud infrastructure, executes the

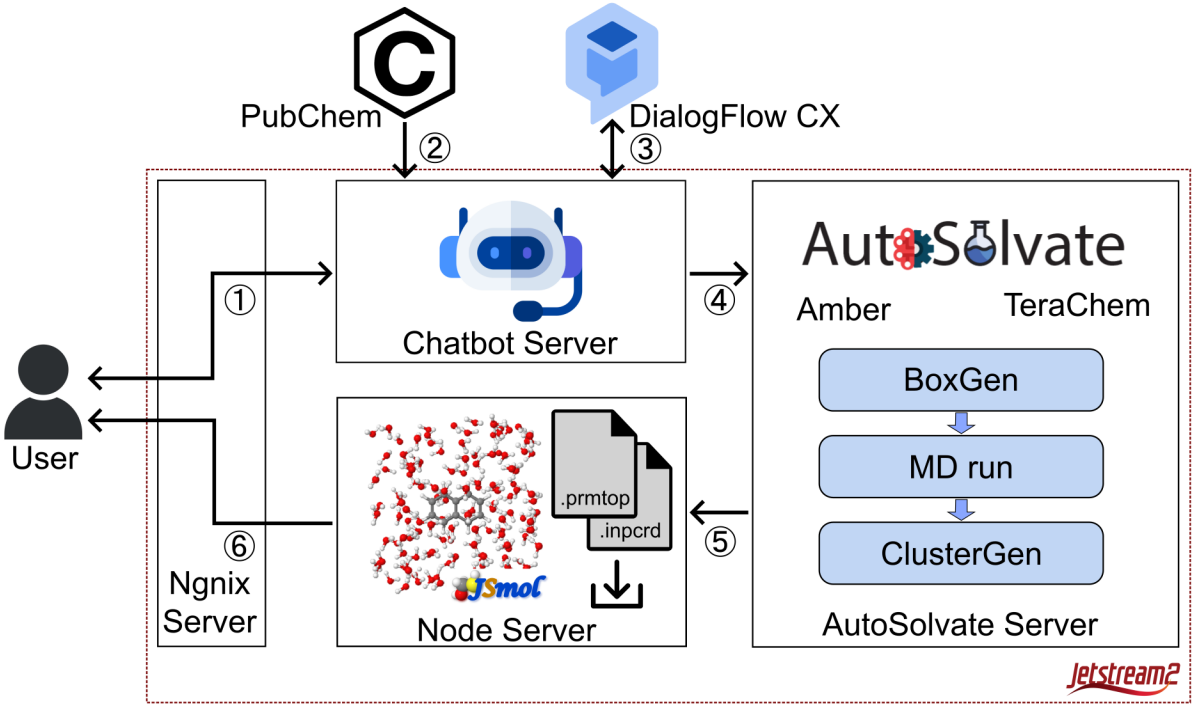

Figure 1. AutosolvateWeb workflow. (1) the user communicate with the chatbot server through the Ngnix server; (2) the chatbot retrieves the required structure from PubChem; (3) the chatbot server making REST API request to the Google's Dialog flow CX virtual agent; (4) the chatbot server sends the necessary information to the AutoSolvate Server and triggers calculation; (5) the results are returned to the Node Server for visualization and downloading; (6) user download the calculation result through the Ngnix reverse proxy.

AutoSolvate workflow with the AMBER[22] molecular dynamics (MD) package and the GPU-accelerated quantum chemistry (QC) package[21], TeraChem.[23] The Node server hosts the webpage with the chatbot frontend and necessary scripts to initiate chat sessions via REST API calls to Google's Dialog flow CX API through the chatbot server. Each user prompt on the chatbot server triggers a REST API request to the virtual agent, facilitating calculation setup via natural language conversations. Once all input parameters are validated and confirmed by the user, automated calculations will be triggered and performed on the AutoSolvate server, with the outputs returned to the Node server upon completion.

Currently, AutoSolvateWeb functionalities align with the AutoSolvate toolkit, covering three main functions: force field and solvent box generation ('Step-1'), MD simulation ('Step-2'), and microsolvated cluster generation ('Step-3'). Solvent boxes, accommodating a user-provided solute molecule surrounded by solvent molecules (water, methanol, acetonitrile, chloroform, or NMA), are constructed using the General Amber Force Field (GAFF).[24] MD simulations utilize AMBER's Sander engine by default. Upon request, QM/MM simulations will be conducted by TeraChem. Finally, users have the option to extract solvated clusters of customized sizes from MD trajectories as inputs for other quantum chemistry packages or workflow. All computations occur on CPU and GPU instances of the JetStream 2 cloud computing platform.

Upon entering the AutoSolvateWeb page, the chatbot greets the user by introducing the three main functions and sequentially guides them through these steps. Figure 2 depicts a sample conversation between the user and the chatbot. In the first step, the user provides the structure by uploading an XYZ file to the chat box or providing the IUPAC name to trigger the chatbot to download the corresponding structure from PubChem. Then, the chatbot navigates the user through the parameter setup procedure by natural language conversation. Buttons with suggested responses are provided in the chat box to simplify this process further. For example, specifying

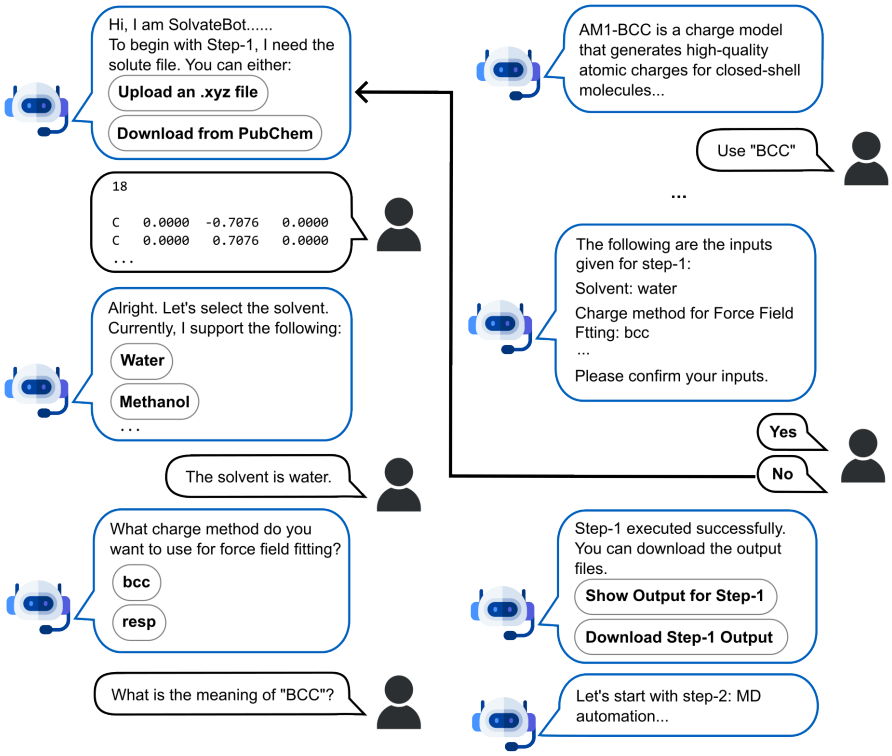

Figure 2. AutosolvateWeb capabilities. The chatbot is able to guide the user through the three-step AutoSolvate Workflow including forcefield and solvent box generation, MD automation (both MM and QM/MM), and cluster generation. A sample conversation for running the Step-1 is shown. The functionality for explaining terminologies to the user will be implemented very soon and it is currently achieved by providing a link to the definition.

the solvent can be done by typing 'water', 'the solvent is water', 'use water', or clicking on the 'water' button in the chat box. Further, while prompting for a parameter, a link to its definition is also provided to the user. Once all parameters are set, the chatbot automatically validates the parameters before confirming with the user to initiate the calculation. At this step, the user can either confirm or reset the input parameters. Upon user confirmation, the chatbot sends all required information to the backend via the chatbot server, initiating the AutoSolvate workflow and awaiting completion of the calculation. A single compressed file containing all essential files for starting subsequent MD simulations is provided for the user to download, with a 3D image of the generated solvent box visualized on the webpage by JSmol.[25] The chatbot then prompts the user to proceed to Step-2 by asking, 'Do MD simulation?' The user can either follow the chatbot to proceed, redo the previous step by typing in 'restart Step-1', or terminate this workflow by saying 'goodbye' or same meaning words. Similar conversations are available for configuring and executing Step-2 and Step-3.

Discussion

AutoSolvateWeb pioneers the use of chatbots to facilitate complex computational workflows in a user-friendly manner, enabling cloud-based, high-throughput solution-phase chemistry data generation. Through interactions with AutoSolvateWeb's chatbot, individuals unfamiliar with MD and QC software can perform multiple-step explicit solvent simulations without delving into lengthy documentation, thus flattening the learning curve for new computational chemistry software and potentially revolutionizing the user experience of advanced scientific tools. Moreover, AutosolvateWeb enables researchers to participate in data generation and sharing without prerequisite computing hardware, democratizing data-driven research in related fields.

As a proof-of-concept tool, AutosolvateWeb still has ample room for improvement. To utilize cloud computing resources more efficiently, AutoSolvateWeb can implement data storage and reuse functionalities. Previously computed data should be stored and indexed on the server with user consent, facilitating future data reuse through keyword- or structure-matching queries. To simulate a broader range of chemical systems, the backend of AutosolvateWeb can be extended to support various organic solvents, mixed solvents, and electrolyte solutions. Certain solutes, such as transition metal complexes and boron-containing compounds, are not yet supported but will be covered in future releases of AutoSolvateWeb.

The AutosolvateWeb chatbot can now clarify terminologies, guide parameters setup, perform fact-checking, and initiate MD and QM calculations. Yet, due to chatbot architecture limitations, users must adhere to a specific sequence of conversations to complete the solvated structure generation. Despite their language input flexibility, chatbots may still misinterpret user requests when their utterances deviate from our predesigned patterns. Large language models (LLMs), featured by the OpenAI's GPT, have consistently demonstrated remarkable versatility in recent years. While training an LLM for field-specific tasks remains data-demanding and computationally expensive, we expect that with advancements in AI, field-specific LLM will be more accessible in chatbot frontend design. Users will be able to perform highly complex calculations using natural language, bypassing predefined steps and patterns.

In conclusion, AutosolvateWeb innovatively integrates a chatbot frontend and cloud computing with automated workflow, significantly reducing the knowledge and hardware barriers in using computational chemistry packages and democratizing data-driven research across the chemical science community. We anticipate the adoption of analogous strategies to incorporate AI across various domains of basic science, transforming the utilization of advanced scientific tools.

Methods

AutoSolvateWeb consists of four containerized applications: a web application, a reverse proxy application, a virtual agent proxy service, and an AutoSolvate cloud server application. Due to robust containerization, all applications can be horizontally scaled seamlessly on both traditional and elastic clusters. All the containerized applications are currently deployed on a single cloud instance (4 cores with NVIDIA A100 GPU) on Jetstream2. [26] Jetstream2 is a user-friendly cloud computing environment facilitating rapid instance creation and future scalability.

Web Application and reverse proxy application. The web application engages with users to authenticate identity, define input parameters and files, and visualize molecular geometry. This service also manages user-specific file storage and facilitates inter-server calls to launch computation jobs. Interactive visualization of input and output molecular geometry files is enabled by the JSMol viewer.[25] SSL ensures the security of all communication between the web application and the user's browser. In addition, strategically positioned CAPTCHA verifications from 'hCAPTCHA'[27] have been integrated throughout the web application workflow to prevent abuse by spam bots. Since all four applications are currently deployed on a single cloud instance, a reverse proxy application using Nginx[28] redirects requests to appropriate applications. Additionally, since a reverse proxy also acts as a load balancer, any future scalability (i.e., deploying to multiple cloud instances) is secured.

Virtual agent. We have employed Google's DialogFlow CX to develop the virtual agent because of the extensive documentation, ease of annotation, and flexibility in designing agent responses. All the interactions between the virtual agent and users rely on a virtual agent proxy service. Apart from handling server-server authentication with Google Cloud Platform (GCP), this proxy service also acts as a gateway to restructure the virtual agent's responses to deliver complex

end-user interaction experiences (such as loading visualizations on job completion and uploading files as part of the conversation) on the webpage.

Conversation in DialogFlow CX is a collection of flows embedded in a finite state machine. Each flow may be made up of multiple pages. Each page may have an entry fulfillment (parameters to be filled in by the user during the conversation) and a route that decides the transition to the next page. Each route is either associated with an intent or some condition (Boolean equation) based on the parameters filled by the user or both. The virtual agent in AutoSolvateWeb has a single flow of twelve pages and six intents. Each of the pages represents a state in the conversation, allowing the user to (1) choose between uploading a solute file or downloading from PubChem API; (2) specify the solute name; (3) upload a geometry file; (4) choose the recommended parameters for the solute in step 1 if the solute is downloaded from PubChem API; (5) set all the solute and solvent parameters manually in step -1; (6) confirm the inputs of step -1; (7) choose if step 2 is to be run in the "dry run mode"; (8) set parameters for MM minimization in step 2; (8) choose to add QM/MM to step -2; (9) set parameters for QM/MM in step 2; (10) confirm inputs for step 2; (11) set parameters for step 3; (12) confirm inputs for step 3. Pages 2, 6, 10, and 12 post webhooks to the Autosolvate web server as part of their fulfillment. Currently, the six intents are to: (1) recognize a successful task; (2) recognize a failed task; (3) recognize a Boolean True input from the user; (4) recognize a Boolean False input from the user; (5) recognize if the user wants to upload the solute file; (6) recognize if the user wants to download the solute file from PubChem. Additionally, there are three more intents corresponding to restarting each of the simulation steps, which are triggered in response to a phrase fuzzy matching the following: (1) 'Run step-1' or 'Restart step -1'; (2) 'Run step-2 [in dry run mode][with QM]' or 'Run step-2 [in normal mode] [with QM]'; (3) 'Run step -3' or 'Restart step-3'. It is worth noting that user prompts need not

match the exact phrase of an intent. DialogFlow CX can map a similar phrase to their respective intents.

Also, all the responses from the virtual agent have a 'recommended response' for the user - except for prompts that ask the user to set input parameters. This aims to familiarize new users with the workflow of the chatbot. The users might also choose to input any of the above-discussed intents to steer the conversation.

AutoSolvate cloud server. Finally, the Autosolvate cloud server application executes the computation job only at the request of the web application or the DialogFlow virtual agent through an authenticated webhook. The containerized image of this application has an Autosolvate Conda environment, all the third-party software (AMBER,[22] GAMESS[29] and TERACHEM[23]) orchestrated by the Autosolvate framework and distributed computing frameworks such as OpenMPI.[30] Hence, this container may be deployed seamlessly on any traditional cluster or a cloud computing instance. The server application has four workers to handle job requests, which are processed synchronously. Each job request spawns a new process to execute the job. Further, the GPU drivers are exposed only to this application.

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Author contributions

F.L. conceived this project. R.S.K.G. designed the cloud computing orchestration architecture. R.S.K.G. and R.M. implemented the frontend web server, supervised by Y.W. and F.L. jointly. R.S.K.G. and S.D. designed and implemented the chatbot. L.D. and F.L. contributed to the code improvement of the backend. F.R., R.S.K.G. and F.L. wrote the first draft of the manuscript, and all authors commented and revised the manuscript.

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