Development of a Software Framework for Formalizing Forcefield Atom-Typing for Molecular Simulation

Janos Sallai, Tengyu Ma, Chris Iacovella, Christoph Klein

janos.sallai@vanderbilt.edu

WSSSPE4, Manchester, UK

Overview

Problem 1: specifying *forcefield* parameters in molecular simulations is a tedious, error prone task, particularly for large systems (lack of automation)

=> State-of-the-art software-engineering techniques to the rescue!

- Model-integrated computing (MIC)
- Domain Specific Languages (DSL)

Problem 2: forcefields are published in books, journal papers, websites of research groups, etc. (data management issue)

=> CI service does domain-specific forcefield verification, catalogs forcefields.

Background: forcefields

Forcefields describe interactions between particles in molecular simulations

- Forcefield parameters depend not only on the particle type (e.g. Carbon or Oxygen atom)

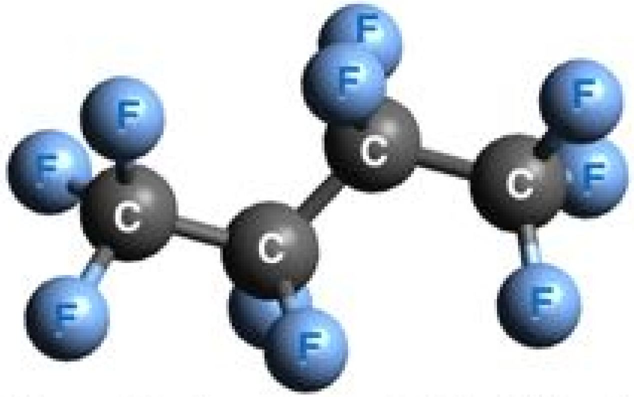
Interaction types	**Force as a function of**
Bonds	Bond distance
Angles	Angle defined by 3 particles
Torsion angles	Torsion angle defined by 4 particles
Non-bonded interactions	Distance of particles

Background: forcefields

Forcefields describe interactions between particles in molecular simulations

- Forcefield parameters depend not only on the particle type (e.g. Carbon or Oxygen atom)

- BUT also on the ***chemical context*** (e.g. a Carbon atoms at the end of an alkane chain different parameters from those in the backbone)



Perfluorobutane CF_3-CF_2-CF_2-CF_3

Background

Today, large molecular systems (inputs to simulators) **are built from recurring blocks**

- Blocks capture **structure** (particles, bonds, etc) **and forcefield** parameters
- Building a system for blocks is done in custom code (Python, C++, etc.)

Background

Today, large molecular systems (inputs to simulators) **are built from recurring blocks**

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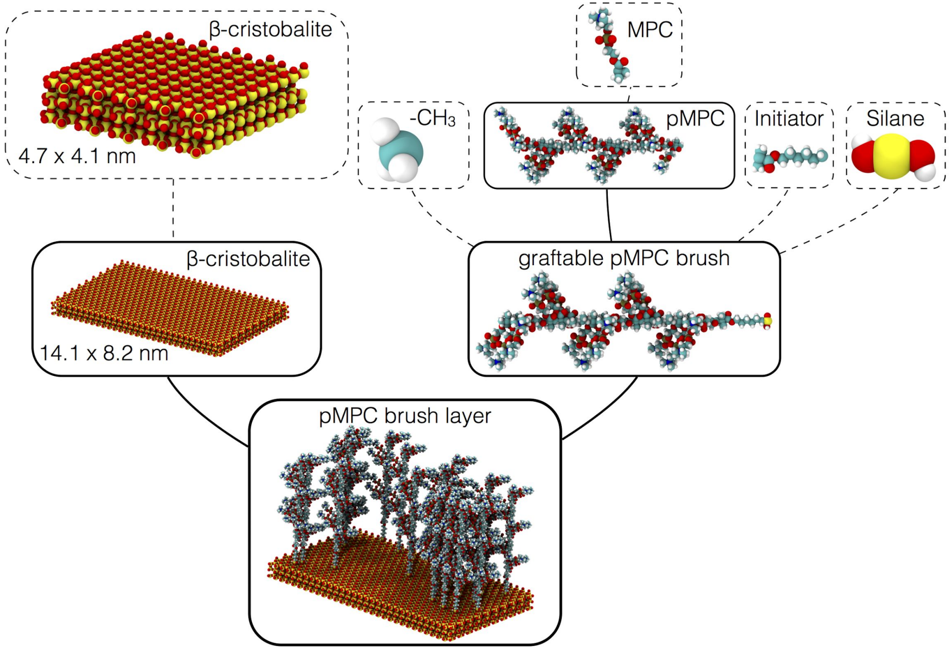
BUT

- **Stitching** blocks together **is hard**
  - There are bonds and other interactions across block boundaries
  - How these are handled depends on the type of the connecting block
- Blocks **cannot be reused** across projects
  - Even if structural building blocks are the same, forcefield used varies from project to project

Separation of structure and forcefield

mBuild creates complex molecular structures from reusable components

- Components are connected with ***ports***
- Ports define geometric relations
- Supports ***hierarchical composition***
- Provides ***generative modeling*** operations (tiling, space filling, grafting, masks)



How should we apply forcefield parameters?

https://github.com/iModels/mbuild

Applying forcefield to structures

We are building a tool to do this ***automatically***.

Foyer: a tool to compute forcefield parameters of a structure

- Reads in structure and specification
- Outputs a structure with forcefield parameters that can be fed to a MD simulator

Foyer’s forcefield definition specifies ***parameters and context*** in which they apply

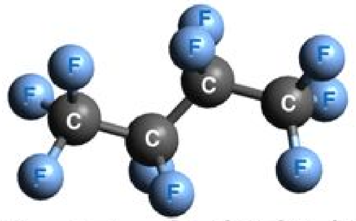
- Context is specified as **logic statement** over graph structures (rules)
- Set of rules can be statically checked to **verify** that
  - Forcefield parameters can be computed unambiguously
  - There are no contradictory rules

https://github.com/iModels/foyer

Forcefield specifications

A table with interaction types the corresponding parameters

```
atom        791   13    CT    "Perfluoroalkane CF3-"     6    12.011    4
atom        792   13    CT    "Perfluoroalkane -CF2-"    6    12.011    4
vdw         791               3.5000     0.0660
vdw         792               3.5000     0.0660
charge      791               0.3600
charge      792               0.2400
```



Perfluorobutane CF_3-CF_2-CF_2-CF_3

Where is it coming from?

- Published in books/journal/conference papers
- Some simulators include forcefield files (tend to be general-purpose)
- Research groups develop in-house forcefields that are designed for a particular class of chemical systems (e.g. proteins, nanolubrication, etc)

Documentation of applicability is often lacking.
Even if documentation exist, it is not machine-readable.

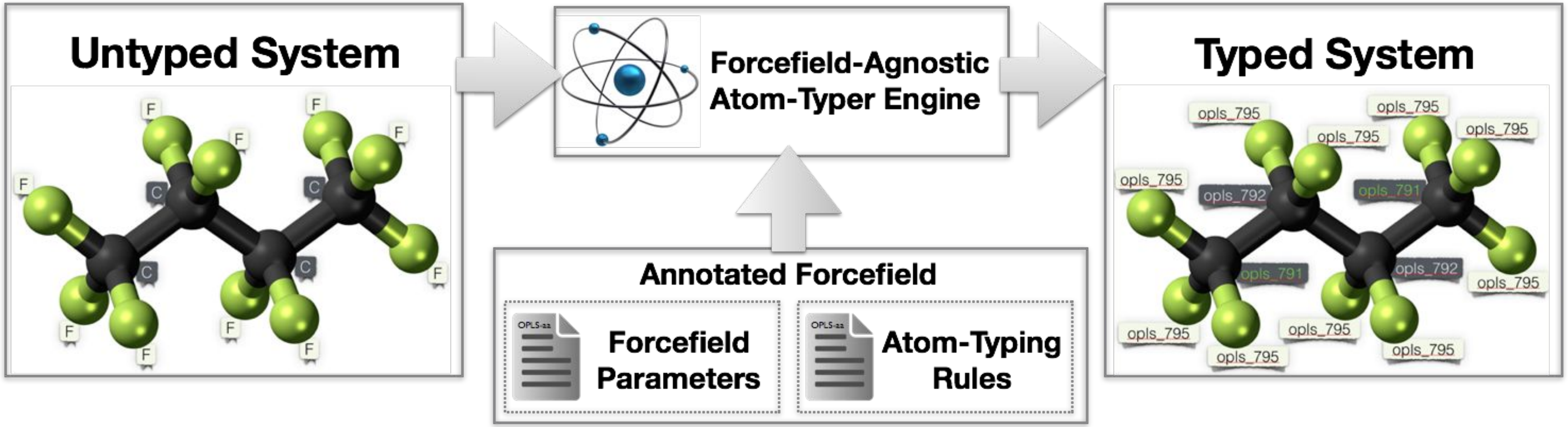
Forcefield specification

Foyer provides a formalism to describe applicability rules.

C_{791}`: type=C & count(bonded atoms(type=F))=3 & count(bonded atoms(type=C))=1`

C_{792}`: type=C & count(bonded atoms(type=F))=2 & count(bonded atoms(type=C))=2`

This has to be done by the developer of the forcefield.



Online forcefield repository

Goals: having an online forcefield repository that

- is searchable
- captures evolution of forcefields (version control)
- links back to external URLs/DOIs that use/reference a particular forcefield
- provides an API for tool integration

This goal is **elusive**. Hard to **incentivize** research groups to contribute.

Forcefield CI

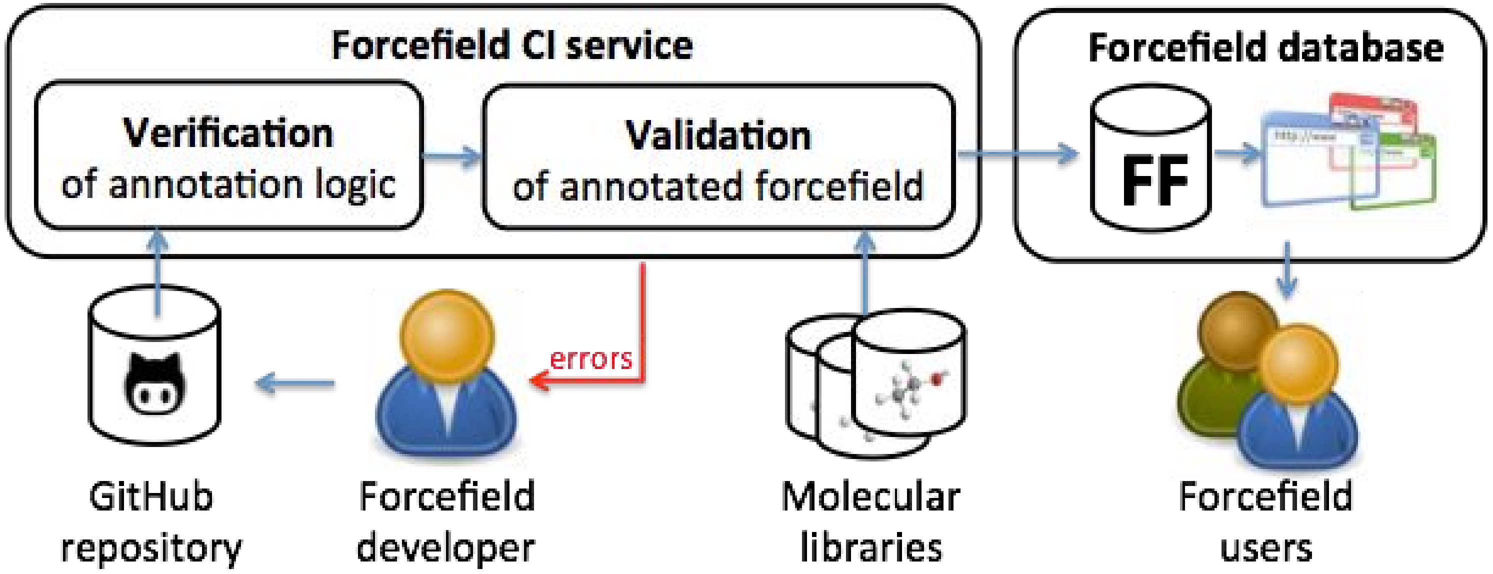
Motivation:

Research groups store forcefield specifications in public repositories such as GitHub. GitHub’s webhooks allow for easy integration.

Validating an annotated forcefields requires test cases. A central database of structures and their known good parameterizations can be used to test multiple forcefields.

CI service can catalog the forcefields that are hosted on GitHub, can can create a searchable database.

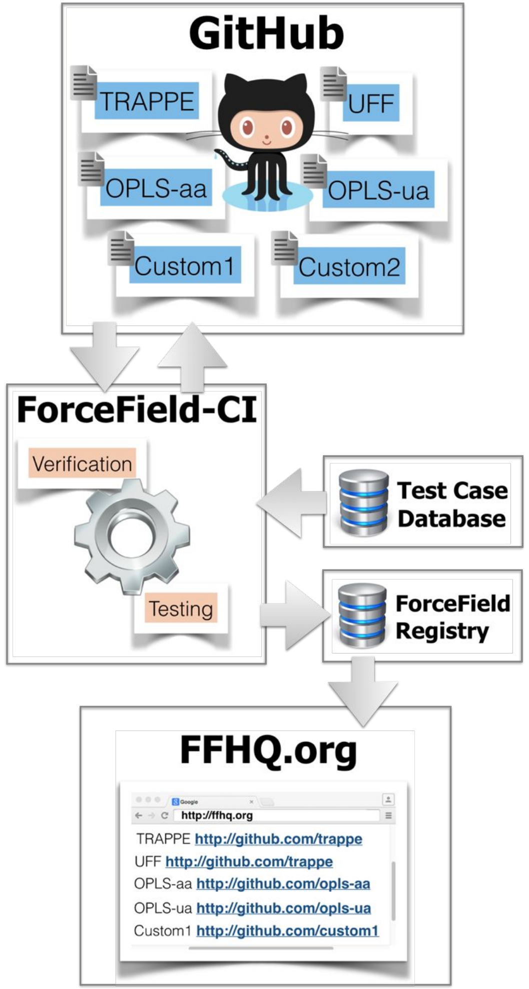
Forcefield CI



Forcefield CI

We are building a Continuous Integration service that

- Integrates with GitHub
  - Webhooks on commits/pull request
- Verifies forcefield specs
  - Ensures unambiguity of rules
  - Reveals conflicting rules
- Validates forcefield specs
  - Runs Foyer on test cases: structures without parameterizations
  - Compares Foyer output with known parameterization
- Reports results
  - Forcefield CI web interface
  - Pass/Fail result to GitHub

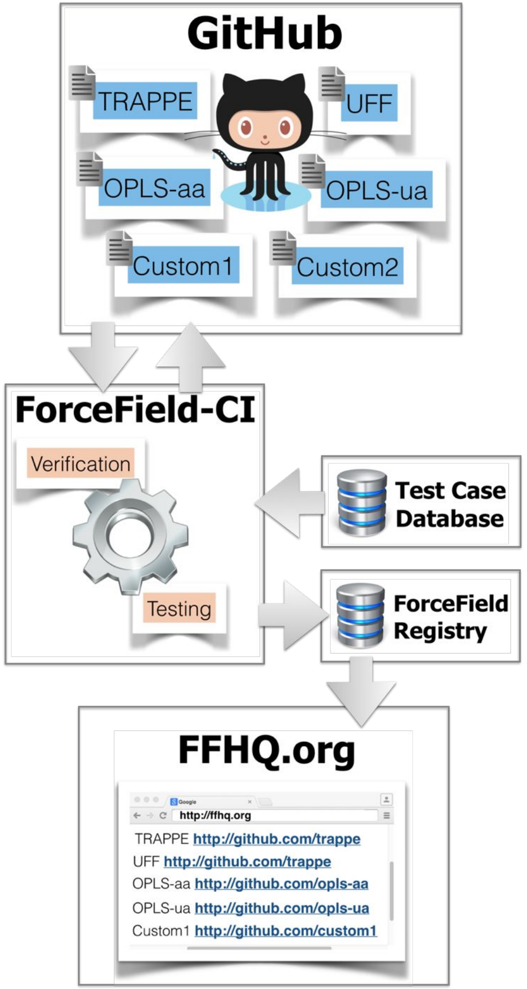


TRAPPE http://github.com/trappe
UFF http://github.com/trappe
OPLS-aa http://github.com/opls-aa
OPLS-ua http://github.com/opls-ua
Custom1 http://github.com/custom1

Forcefield CI

Our team is building an online Continuous Integration service that

- Maintains a database of forcefield projects
  - Follows how the forcefield evolves
  - Maintains history
  - Provides an online, searchable interface
- Assigns permalinks to forcefield versions
  - Unique, stable URI (and URL) for each git commit that contains forcefield change
  - We consider assigning DOIs
- Maintains back references
  - Links from forcefield to projects where it is used



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Status

mBuild: building complex molecular structures through component composition

- Production ready
- Available at https://github.com/iModels/mbuild

Foyer: assigning forcefield parameters to untyped structures

- Prototype ready: https://github.com/iModels/foyer
- Small subset of OPLSaa forcefield works
- Declarative annotation syntax is being developed

Forcefield CI

- Web application, GitHub integration prototype is ready
- Verification, Validation, Forcefield catalogization is in planning phase

Questions

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janos.sallai@vanderbilt.edu