RepEx: A Flexible Framework for Scalable Replica Exchange Molecular Dynamics Simulations

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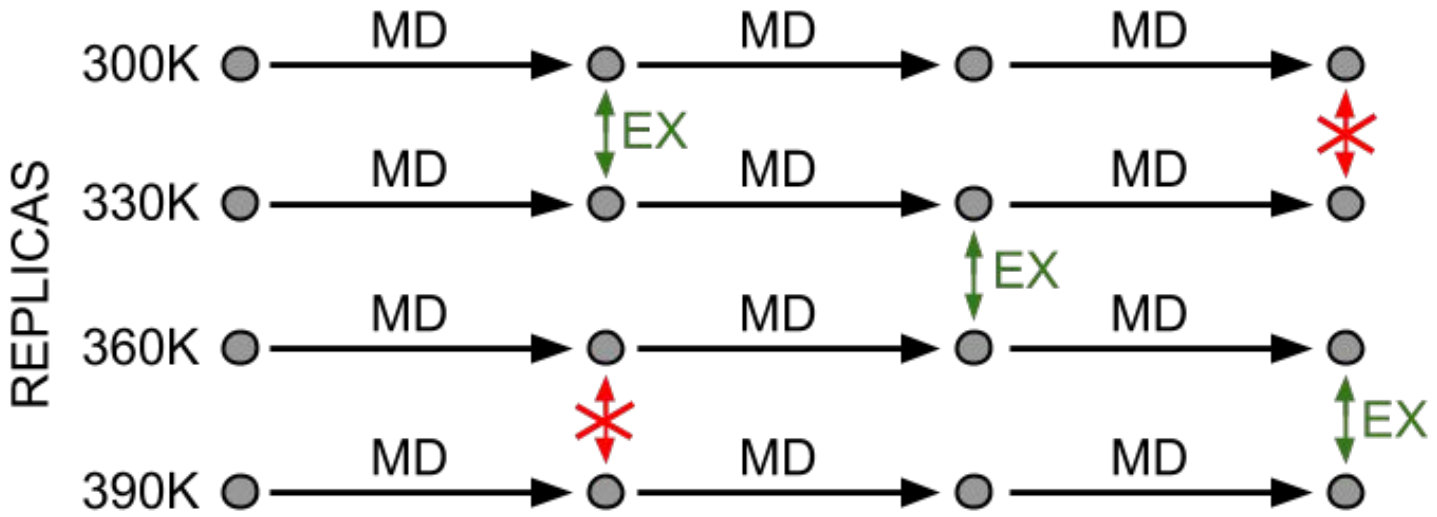
Outline

- What is replica exchange?
- Why replica exchange?
- Current challenges in REMD software
- Our contribution
- RepEx design principles
- Performance characterization
- Why RepEx?
- Conclusion

What is replica exchange?

- Replica Exchange Molecular Dynamics (REMD)
- Introduced by Sugita and Okamoto in 1999 [1]
- The algorithm:
  - Concurrently run multiple Molecular Dynamics (MD) simulations at different temperatures for N time-steps
  - Select exchange partners: neighbours, all, etc.
  - Accept exchange of temperatures according to probability given by the Metropolis criterion
  - Repeat

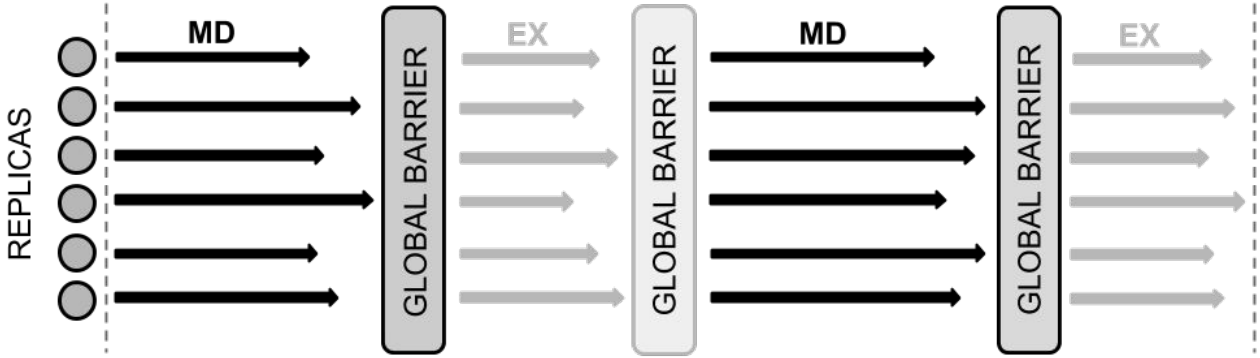
What is replica exchange?



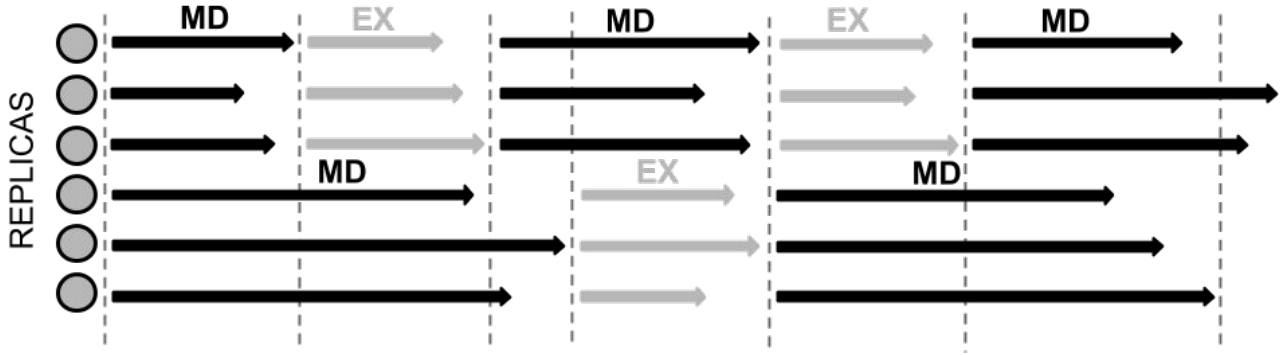
Why replica exchange?

- Protein structure prediction and protein design
  - understand how protein works to target it with drugs
- Role of proteins in diseases
  - HIV virus
  - Cancer
  - Alzheimer’s

Synchronization in Replica Exchange



Top: Synchronous RE; Bottom: Asynchronous RE



Current challenges in REMD software

- REMD capability is integrated into molecular simulations software
  - advances in the RE methodology are tied to the particular MD code
  - can't take advantage of the advances in other MD simulation engines
  - high barrier for addition of different exchange parameters
  - high barrier for implementation of REMD algorithms
- Synchronization flexibility
- Fault tolerance

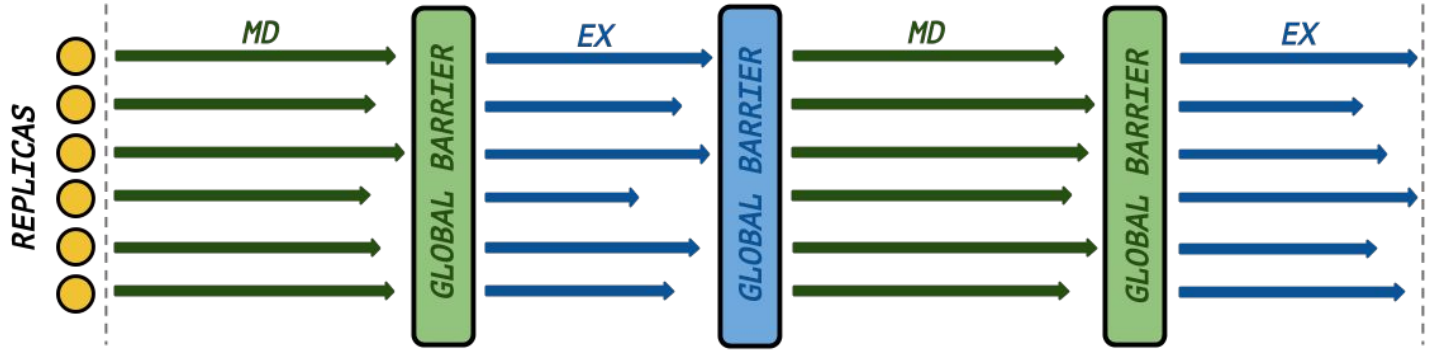
Our Contribution

- RepEx package
  - Allows to run multi-dimensional RE simulations
  - Enables implementation and testing of various RE methods
  - Can be extended to use any exchange parameter and/or MD engine
  - Supports synchronous and asynchronous RE
- “Ensemble of tasks” solution to a set of challenges associated with RE implementations

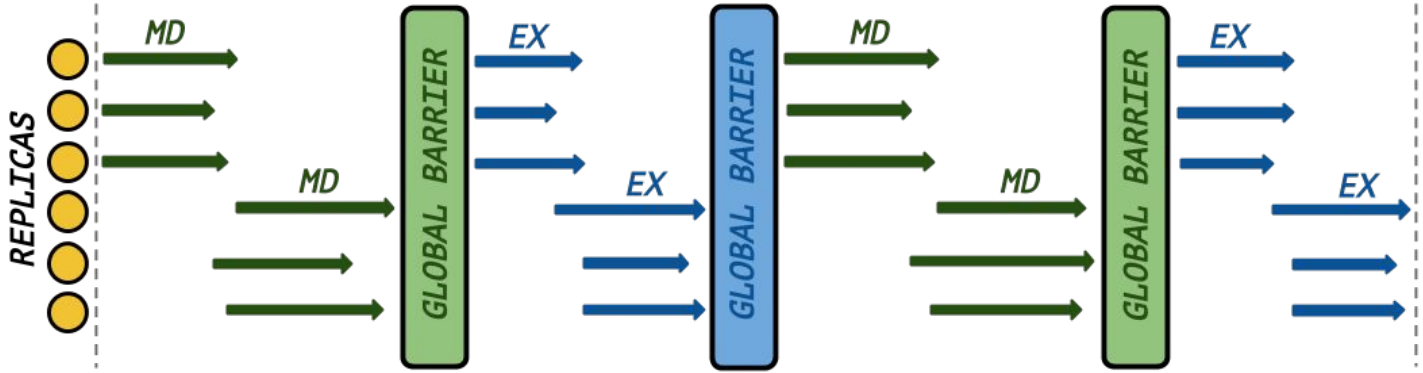
RepEx: Pilot System

- A multi-stage mechanism for workload execution via the use of a placeholder job
- Execution and management of workloads with multiple, heterogeneous and dependent tasks
- RADICAL-Pilot
  - API in Python
  - > 100 tasks/second
  - < 8000 concurrent tasks
  - Portability across various HPC architectures
  - Explicit support for synchronization

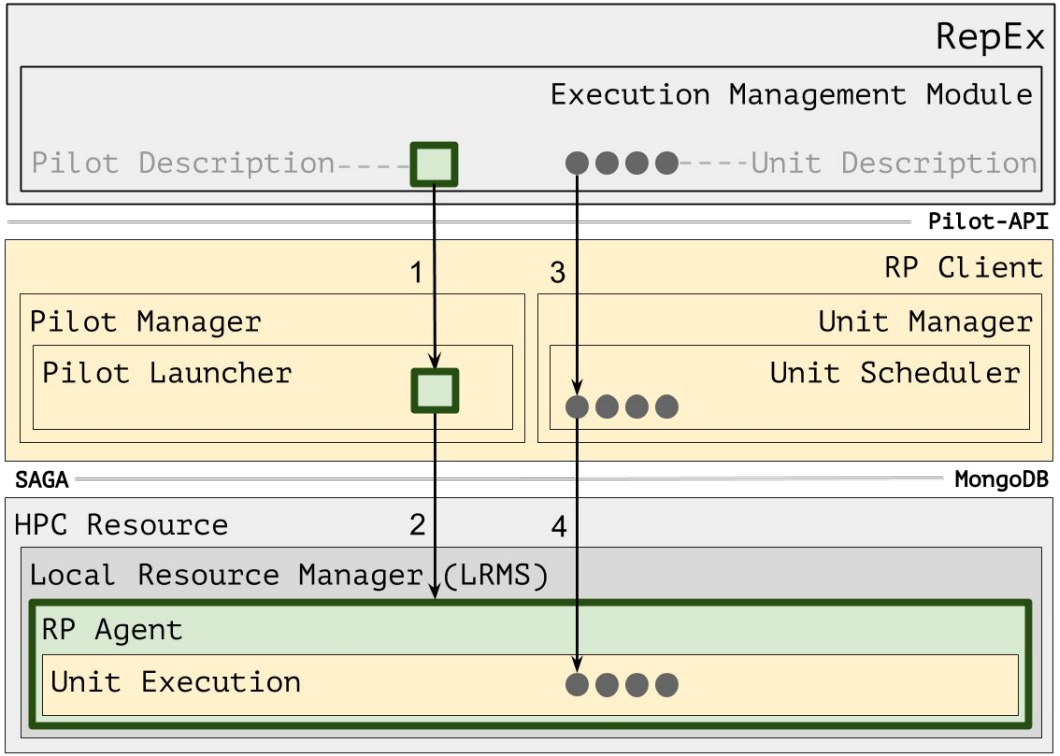
RepEx: Flexible Execution



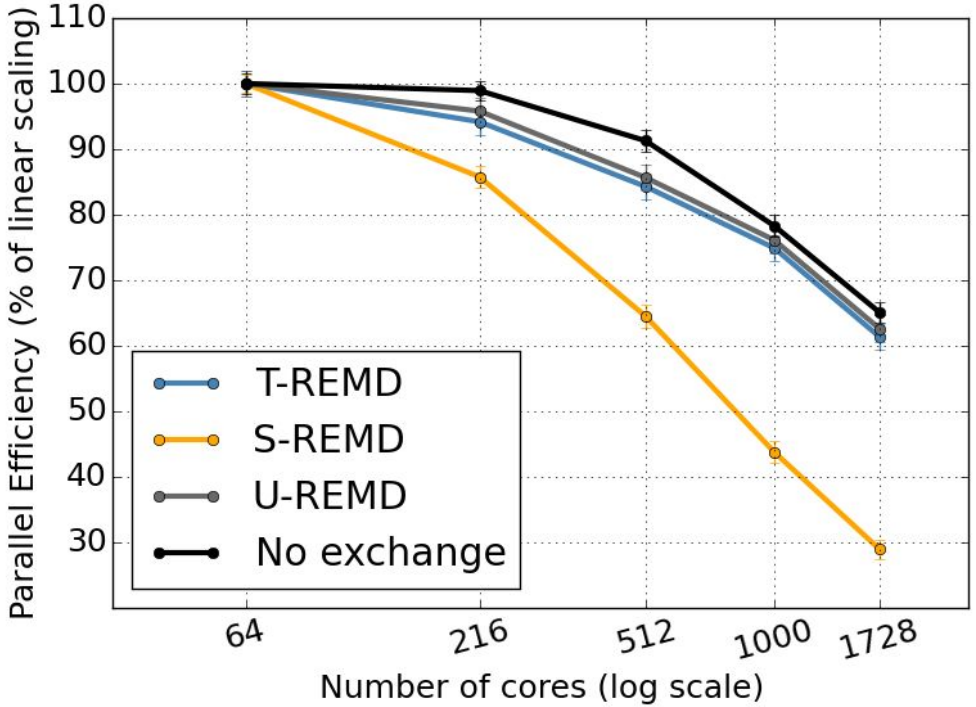
Top: Execution Mode I; Bottom: Execution Mode II



Task Execution Diagram



Performance characterization



Weak scaling parallel efficiency (% of linear scaling) for temperature exchange (T-REMD) , salt concentration exchange (S-REMD) and umbrella exchange (U-REMD). For all simulations is used alanine dipeptide. We perform 6000 simulation timesteps between exchanges. Runs are performed on SuperMIC cluster using Amber MD engine.

Why RepEx?

- Satisfies functional, performance and usability requirements of the REMD simulation software
- No limitation in the number and ordering of dimensions for M-REMD simulations
- Explicitly supports sync. and async. RE
- Can be extended to support other MD engines with minimal changes at the source code level

Why RepEx?

	Amber	GROMACS	LAMMPS	VCG async	CHARMM	Charm++/ NAMD MCA	RepEx
Max replicas	~2750	~900	100	240	4096	2048	3584
Max CPU cores	~5500	~150000	76800	1920	131072	524288	13824
Fault tolerance	n/a	n/a	n/a	basic	n/a	n/a	basic
MD engines	Amber	Gromacs	LAMMPS	IMPACT	CHARMM	NAMD	Amber, NAMD
RE patterns	sync	sync	sync	sync, async	sync	sync	sync, async
Nr. Exec. Modes	1	1	1	2	1	1	2
Nr. dims	2	2	2	2	2	2	3
Exchange params	3	2	2	2	2	2	3

Conclusion

- Task level parallelism approach:
  - Helps to overcome challenges faced by REMD software packages
  - Lowers the barrier for development and testing of various REMD methods
- RepEx serves as an umbrella for MD engines developed by different scientific communities

References

1. Sugita, Yuji, and Yuko Okamoto. "Replica-exchange molecular dynamics method for protein folding." Chemical physics letters 314.1 (1999): 141-151.
2. RepEx, https://github.com/radical-cybertools/radical.repex
3. RADICAL-Pilot, https://github.com/radical-cybertools/radical.pilot
4. Chodera, John D., and Michael R. Shirts. "Replica exchange and expanded ensemble simulations as gibbs sampling: Simple improvements for enhanced mixing." The Journal of chemical physics 135.19 (2011): 194110.