



HPC Response to the COVID-19 Pandemic: Introduction

David Keyes

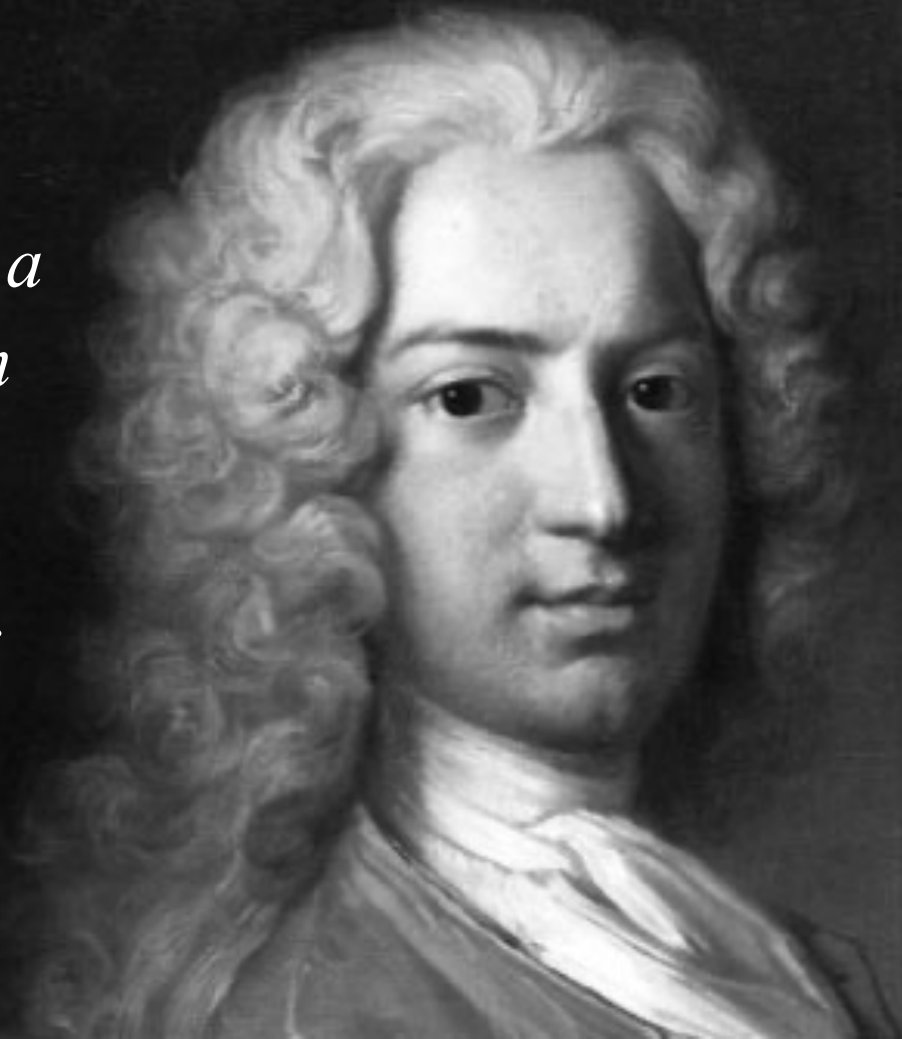
Extreme Computing Research Center (ECRC)

King Abdullah University of Science and Technology



... Paris 1760 ...

“I simply wish that, in a matter which so closely concerns the wellbeing of the human race,



no decision shall be made without all the knowledge that a little analysis and calculation can provide.”

Daniel Bernoulli's analysis of smallpox

*Essai d'une nouvelle analyse de la mortalité causée par la
petite vérole & des avantages de l'inoculation pour la
prévenir*

*(An attempt at a new analysis of the mortality caused by smallpox
and of the advantages of inoculation to prevent it)*

Logistic ODE precursor
of SEIR model

$$-ds = \frac{sdx}{n} - s \frac{d\xi}{\xi} - \frac{ssdx}{mn\xi}$$

x : time
 s : susceptibles
 ξ : survivors
 $1/n, 1/m$: rate constants

presented at
The Royal Academy of Sciences in Paris
on 16 April 1760
published in
Histoire et Mémoires de l'Académie Royale des Sciences de Paris,
1766, pp. 1-45

... March 2020 ...

- COVID19 HPC Consortium established by DOE, NSF, industry, and academia in the US
- COVID19 Fast Track established by PRACE in the EU

... April 2020 ...

- Fugaku brought into service a year early by RIKEN and MEXT in Japan expressly to fight COVID19

... June 2020 ...

ISC 2020 DIGITAL AGENDA, JUNE 22 – 25



from 5 pm

Focus Session

Covid 19 & HPC/AI ▼

Presentations:

Japan and Fugaku's Fight Against the COVID-19 in HPC

Speaker: Satoshi Matsuoka



Supercomputing, COVID-19 and the Transformation of Medicine

Speaker: Peter Coveney



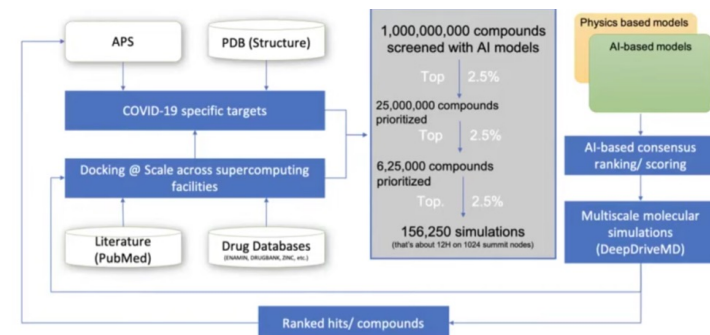
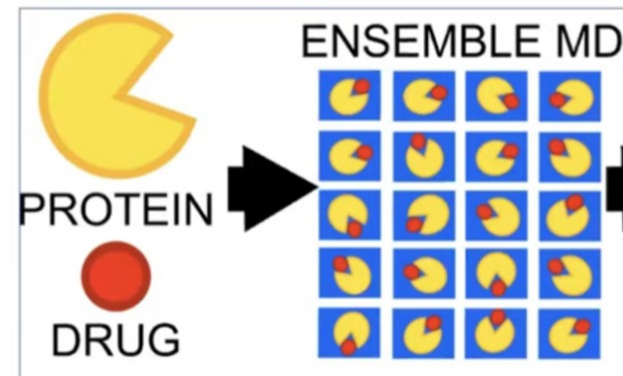
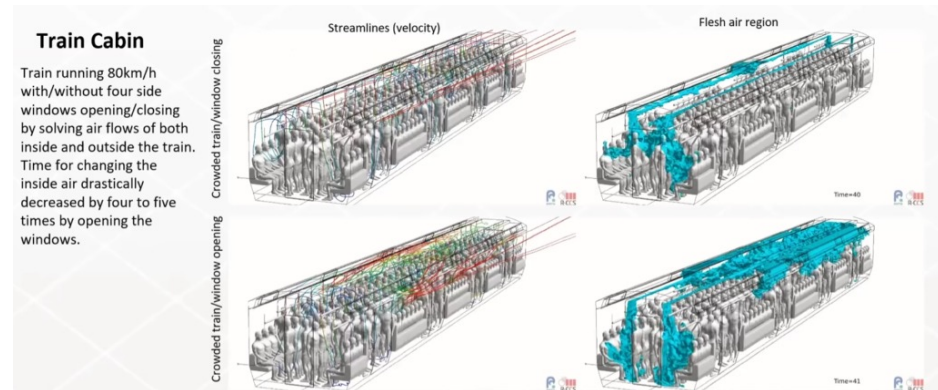
Overview of HPC and AI Computing for COVID-19 in the US

Speaker: Rick Stevens



... June 2020 ...

HPC wire



... June 2020 ...

“COVID19 has had considerable positive impact on CSE research but not *vice versa*.”

“COVID19 understanding and mitigation is still essentially a wet lab and clinical story.”

“Where has CSE had an impact beyond research frontiers – in policy support, diagnosis, or therapy?”

... September 2020 ... *

“Recent results highlight the importance of **computational science as a guiding tool that helps in uncovering the structure and mechanics of the viral spread as well as drastically reduces the number of candidate treatments that need laborious laboratory testing**. From transformative medical advances to drug discovery driven by massively parallel supercomputing, this minisymposium will span a range of practical approaches to the ongoing crisis.”

***from the abstract of SIAM CSE minisymposium**

... March 2021 ...

Report Card		
Subject	Grade	Notes
Visualization	A	virus geometry
Molecular dynamics	A	virus mechanisms
Fluid-dynamical transport	A	safety protocols
Diagnosis	A	clinical accuracy
Drug repurposing	I	efficient trials
Tracking spread & variants	I	understanding scope
Forecasting spread	I	planning resources
Optimizing response	I	setting policy

... November 2021 ...

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Summary (1): CSE has been good for COVID19

- Allowed scientists to visualize hundred million-atom biomolecular clusters in far greater detail than any laboratory imaging system
- Allowed scientists to understand the ACE2 “attack” configuration of the spike protein with its glycan “kickstand” supports
- Allowed health & safety experts to understand convective and diffusive transport of the virus in rooms and passenger vehicles
- Gave clinicians new AI-assisted CT scan interpretation
- Identified hundreds of potential new drugs computationally and launched dozens into experimental pipelines and clinical trials
- Created computational infrastructure and workflows relevant to future pandemics
- Enabled public policy makers to smartly dial the balance between losing lives and suspending livelihoods

Summary (2): COVID19 has been good for CSE

- Pushed #1-ranked system into broad use a year ahead of schedule
- Created new intercontinental HPC consortia
- Led to sharing of data on unprecedented scale
- Created new computer-to-laboratory pipelines
- Focused new attention on the role of preprint archives
- Accelerated injection of AI into scientific and clinical workflows
- Accelerated development of new algorithms in MD
- Accelerated development of new models in epidemiology, population-stratified beyond the classical S-E-I-R, and Bayesian methods in their parameter fitting
- Brought billions of readers and viewers to the precipice of computational modeling and machine learning, “looking in” from popular media accounts; has inspired future scientists

Launched a new Gordon Bell Prize (2021 entries)

- Digital Transformation of Droplet/Aerosol Infection Risk Assessment Realized on Fugaku for the Fight against COVID-19
- Language Models for the Prediction of SARS-CoV-2 Inhibitors
- Data-Driven Scalable Pipeline Using National Agent-Based Models for Real-Time Pandemic Response and Decision Support
- AI-Enabled Multiscale Computational Microscopy of Delta SARS-CoV-2 in a Respiratory Aerosol
- FEP-Based Large-Scale Virtual Screening for Effective Drug Discovery against COVID-19
- Intelligent Resolution: Integrating Cryo-EM with AI-Driven Multi-Resolution Simulations to Observe the SARS-CoV-2 Replication-Transcription Machinery in Action

Molecular Dynamics (R. Amaro, UCSD)

AI-Driven Multiscale Simulations Illuminate Mechanisms of SARS-CoV-2 Spike Dynamics

Lorenzo Casalino^{1†}, Abigail Dommer^{1†}, Zied Gaieb^{1†}, Emily P. Balfanz¹, Tomasz Sztain¹, Surl-Hee Ahn¹, Anda Trifan^{2,3}, Alexander Brace², Anthony Busetto⁴, Hong Ma⁴, Hyungro Lee⁵, Matteo Turilli⁵, Syma Khalid⁶, Lillian Ching⁴, Carlos M. Dominguez⁴, David J. Hardy³, Julio C. Maia³, James C. Phillips³, Thoreten Furtak⁸, Abraham Stern⁸, Lei Huang⁹, John M. Calvert⁷, Mahidhar Tatineni¹⁰, Tom Gibbs⁸, John E. Stone⁵, Shantenu Jha⁵, Arvind Ramanathan^{1*}, R. Amaro^{1*}

¹University of California San Diego, ²Argonne National Lab, ³University of Illinois at Urbana-Champaign, ⁴University of Pittsburgh, ⁵Rutgers University & Brookhaven National Lab, ⁶University of Southampton, ⁷Stony Brook University, ⁸NVIDIA Corporation, ⁹Texas Advanced Computing Center, ¹⁰San Diego Supercomputing Center, ^{*}Joint first authors. Contact authors: ramaro@ucsd.edu, ramanathana@anl.gov

ABSTRACT

We develop a generalizable AI-driven workflow that leverages heterogeneous HPC resources to explore the time-dependent dynamics

'20: International Conference for High Performance Computing, Networking, Storage, and Analysis. ACM, New York, NY, USA, 14 pages. <https://doi.org/finalDOI>

- **Scientific merits: investigation of SARS-CoV-2 spike protein mechanism**
 - Elucidate invisible mechanisms, including glycan shield and glycan modulating role
 - Classical explicit Molecular Dynamics on 305M-atom viral envelope (up to 4.2 μ s)
- **Infrastructure merits: efficiencies applied at new scales on several large systems**
 - Algorithmic: weighted ensemble strategy in MD – efficiently kill uninteresting trajectories using ML over many short parallel sims parallel, vs. one long serial sim
 - Software: wide portability across new architectures (CHARM36, NAMD2.14)

Molecular Dynamics (R. Amaro *et al.*)

“Computational microscopy”

1. *Spike protein of 600K atoms an order of magnitude larger than previous (100TB per sim)*
2. *Composite system to view “handshake” has 8.5M atoms with explicit water*
3. *Full protein envelope has 305M atoms*

Linked in AI-driven workflow

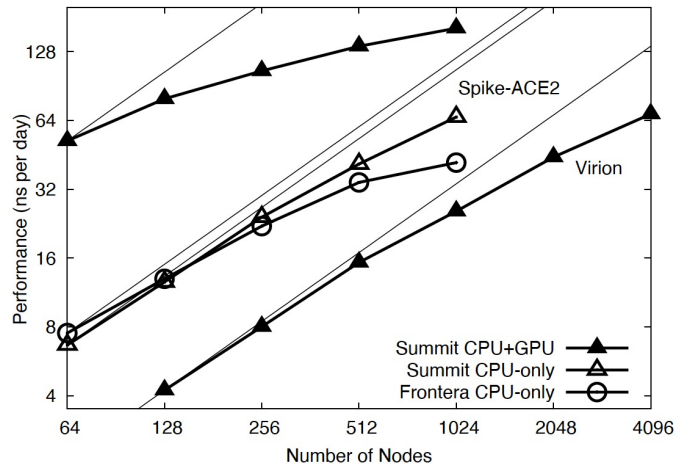
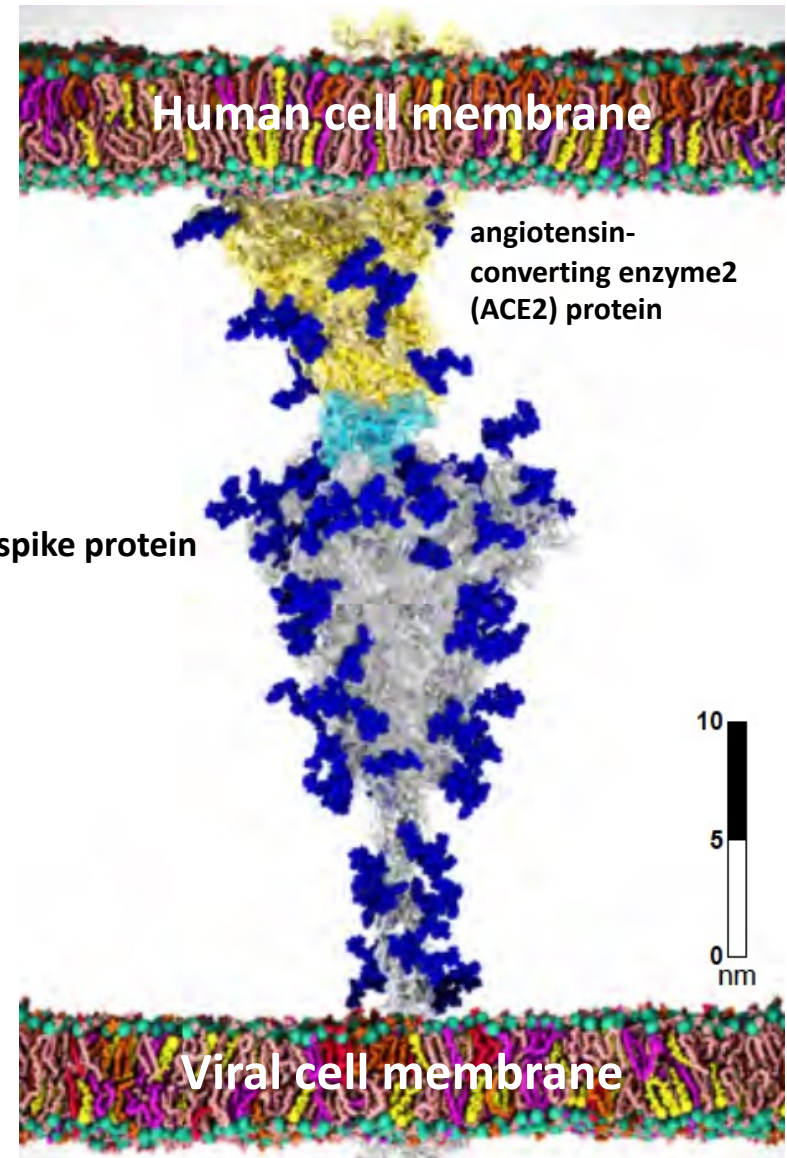
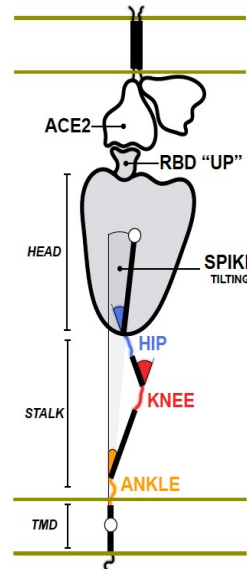


Figure 4: NAMD scaling on Summit and Frontera for 8.5M-atom spike-ACE2 complex (upper lines) and 305M-atom virion (lower line). Thin lines indicate linear scaling.



Aerosol Dynamics (M. Tsubokura *et al.*)

DIGITAL TRANSFORMATION OF DROPLET/AEROSOL INFECTION
RISK ASSESSMENT REALIZED ON "FUGAKU" FOR THE FIGHT
AGAINST COVID-19

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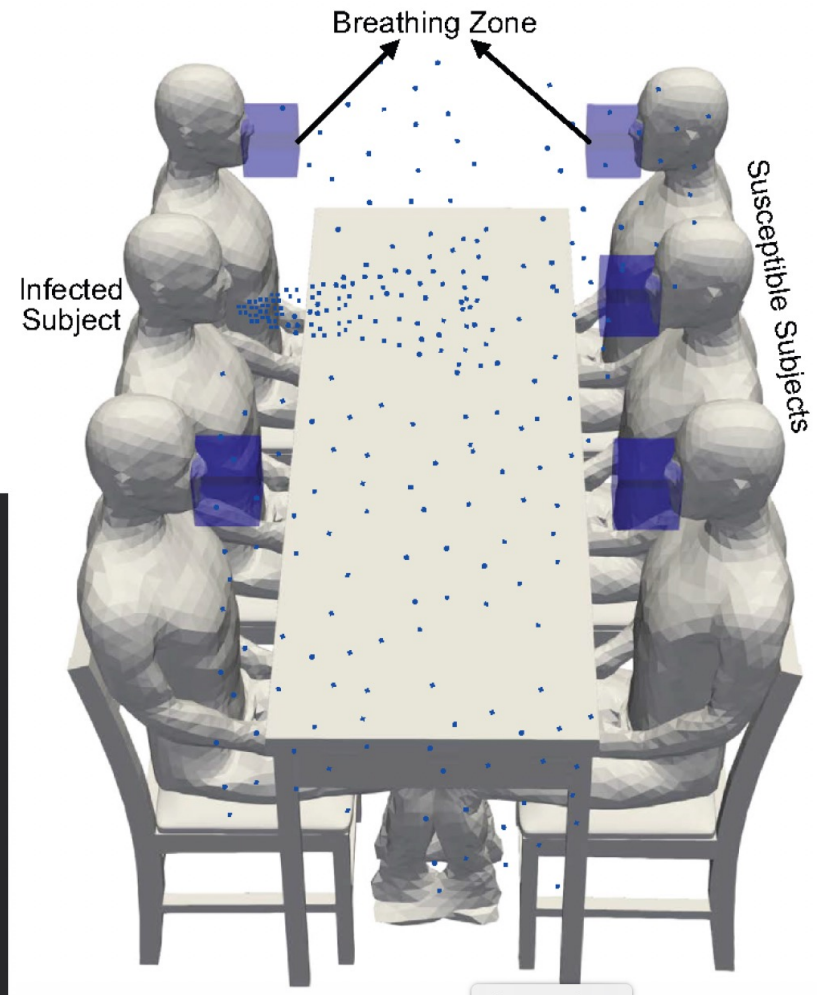
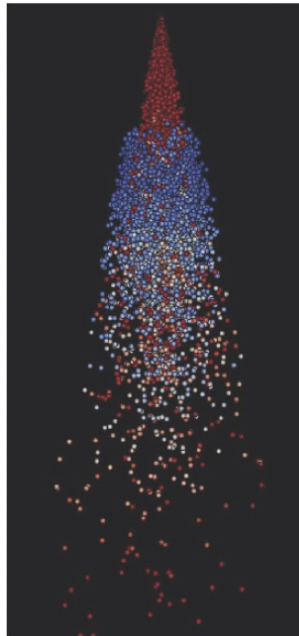
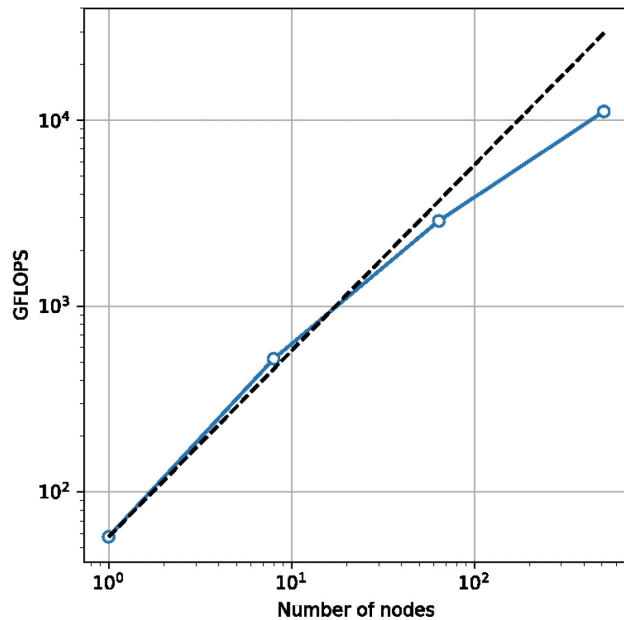
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Aerosol Dynamics (M. Tsubokura *et al.*)

“Computational social policy”

1. *1000's of societal interactions evaluated*
2. *Ill-suited for experiments*
3. *Pivoted from high fidelity droplet simulations in other fields, e.g., spray ignition*

Created new expectations for HPC simulations within entire society



AI is a vital part of the mix

- Allowed MD modelers to “fast forward” over uninteresting stretches of dynamics and to stitch together models at different scales
- Allowed expensive simulation kernels to be replaced with inexpensive input-output functional maps, leading to improved throughput
- Improved on human accuracy, shrinking both false positives and false negatives in clinical tests
- Allowed “most likely” drug candidates to be identified out of billions of compounds after being trained on a small sample of the compounds for their ability to dock on human cell receptors

Summary (3): COVID19 has been good for CSE 😊

“The pandemic hibernation has made the engine lab useless and thus many of my students have converted to simulations. That has more than doubled the use of high-CPU simulations. I do not see this change back to more experiments any time soon...”

– a combustion colleague

Thank you!



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