CINECA's Carlo Cavazzoni Describes the Supercomputing Battle Against COVID-19

The latest episode of the This Week in HPC podcast features Carlo Cavazzoni, a senior staff member at CINECA, one of the leading supercomputing organizations in Europe. Intersect360 Research’s Addison Snell spoke to Cavazzoni to discuss both CINECA’s work using supercomputing to combat COVID-19 and Cavazzoni’s personal experience living near the epicenter of the Italian coronavirus outbreak. We present this lightly edited transcript alongside the podcast audio.

Addison Snell: CINECA is one of the leading supercomputer sites in Europe – in the world, really – and is located in Italy, near the major outbreak of the coronavirus. CINECA is the host of the Marconi supercomputer, which is one of the top 20 most powerful supercomputers in the world, according to the most recent Top500 list. It's been selected as one of the pre-exascale sites for the Leonardo supercomputer, expected to begin arriving at the end of 2021 and go into full production in 2022. Carlo, thank you very much for joining me on a special episode of This Week in HPC.

Carlo Cavazzoni: Hello, Addison! And actually, Leonardo is expected, hopefully, at the beginning of 2021.

Snell: It’s been upgraded since I started talking, so I appreciate you fixing me on that. But more importantly, CINECA has a lot of supercomputing resources available, of course, and has been tapped for a special project by the European Commission, receiving a
grant under a project called “Exscalate” for coronavirus. Can you talk a little bit about that?

Cavazzoni: This is a research project that gets together a lot of the research communities around Europe working on drug design. All these communities are getting together because of the spread of the virus and responding to the urgent call of the European Commission, which funds research on that matter and tries to organize the communities around the research that is needed to find a new drug.

Besides the sad situation, it is really exciting to be part of this endeavor, and all these research teams around Europe have been working together in this consortium. We are committing many more resources than we are receiving, actually, because we feel the urgency to find a solution for the spread in this critical situation. I find a really, really amazing collaborative spirit among different sites – we have CINECA, but we also have Barcelona Supercomputing Center [BSC], we have Jülich Supercomputing Centre, we have the KTH supercomputing center... All the research teams working around these supercomputing centers – the researchers and the scientists – are sharing knowledge, working together, to ensure that we get the fastest possible good candidate drug for the coronavirus.

Snell: Inasmuch as there’s a new grant responding to this urgent outbreak worldwide, this is actually not starting from zero, right? We actually had a project or some infrastructure in place previously studying the Zika virus.

Cavazzoni: Yeah, actually, in a bad situation we were lucky to be ready for that since all of the machinery was the outcome of a previous European-funded project that was called ANTAREX, where we were able to bring all the codes and workflows from small-scale contexts to the supercomputing infrastructures. So this was ready a year ago, it has been tested on the Zika virus – nothing that was such an emergency as we have right now – so we were ready and we’ve been working for one month on having the platform up and running on our supercomputer. So we were definitely not starting from zero, and if you take into account the development – the early stages of the codes and the workflow – that dates back to 2005, when we started to understand that in drug design, supercomputing may have a role in the future. And now we are in that situation.

Snell: You in particular are an expert in chemistry. You’re one of the primary developers of the Quantum ESPRESSO code, which is one of the top ten most-cited applications in the chemistry field in our [Intersect360 Research] site census survey worldwide, chemistry of course being the broadest HPC area in terms of applications named. You’re not necessarily an expert in coronavirus specifically, but this is in part a public-private partnership that brings in not only these resources from BSC and Jülich like you already described, but also some work with [pharmaceutical company] Dompe locally, so there’s a lot of expertise being brought to bear in this project.
Cavazzoni: Yes, my background is in material science and my main development is in quantum chemistry codes, and so in this particular case, my expertise is related to the competence of bringing applications from low-end to high-end. So besides the HPC specialists, actually, most of the researchers are from the pharmaceutical industry, working really hard, almost 24 hours a day, and from other research labs in Europe that are not linked directly to the supercomputing center. We have a research lab in Switzerland, we have hospitals, we have facilities in Belgium for *in vitro* testing of the molecules we will suggest. So most of the researchers involved are experts in the field, while HPC is an enabling infrastructure and provides the competence that can speed up what would previously take months or years: having the candidate molecules to be handed over to the labs, where they have to synthesize the molecules and test in biological environments and then, finally, prescribe to humans. So we will shorten this initial stage to almost zero time because we are talking about weeks... even if, when are you on the spot, that seems not to be zero time.

Snell: This is something that's moving very quickly of course, and we're going to talk about that in a minute, but first let's drill down a little bit on the use of HPC and AI. You were mentioning some of the work that goes on there, and as an analyst, I can think through a lot of the myriad ways that HPC or AI could be used in terms of helping with the scientific study of the spread of a pandemic. And with COVID-19, we could be looking at exactly that: monitoring, or better yet, predicting the spread from the source, how it moves through a community. Then there's what you were just talking about, genetic sequencing, understanding how the molecule works and the science behind it. Moving that up toward treatment or mitigating the effect of the disease, plans for prevention, plans for a cure, ultimately the design of drugs or a vaccination looking forward.

Now, you're not involved in *all* of those areas in terms of chemistry right now, but can you talk about some of the specific applications you're using and where your research is fitting in to help the world cope with COVID-19?

Cavazzoni: In our pipeline, there are essentially two main kinds of applications. One is molecular dynamics, which we use to properly define and refine the 3D structures of the protein target for the candidate drugs. For that, we use GROMACS code – in fact, we also have Erik Lindahl, who is the main author of GROMACS, as part of this endeavor as well. Then, for the other application, we use molecular docking, which means taking a huge amount of drug candidate molecules and trying to bind those molecules to a digital model of the protein.

So we have all the proteins of the virus that have been identified based on the genomic analysis and homology modeling, all these techniques that require mainly molecular dynamics, and then we are applying this kind of drug design which takes up combinatorial, phase-based exploration of all the configurations of all the candidate drugs and finds out the best candidate in terms of score. And finally, we will refine the score and deliver the best candidate to the labs, because the labs cannot treat hundreds
or millions of molecules, but they can handle in the order of thousands. So we have to
give them the best 1,000 candidate molecules to be tested in the labs. And this is the
challenge we have.

**Snell:** That kind of target reduction has been one of the main application areas that we
found in biosciences in general. It's not practical to look at millions of candidates like you
said, but if we can get that down into the order of a thousand or fewer, that's something
that we can work with and really try to speed this up toward production, and I'm very
appreciative of the work that's being done there.

One of the reasons I like talking to you about this in particular is not just your critical
work on the science, but just at a personal level, you're in one of the most affected areas
in the world. Neither one of us is in Wuhan, China, of course – but in Italy, CINECA is in
Bologna, which is not too far from the epicenter, but you're all working from home, now.
You're in Modena, which is quite close to the original epicenter in Italy; I'm in Silicon
Valley, which is one of the hotbeds in the United States right now. Our schools are still
open for the moment, but things are still changing day-to-day and people are talking
about the United States being only a few weeks behind Italy on the path in terms of this
outbreak. Can you talk just a little bit about your personal experience and how you've
seen the virus spread through your community?

**Cavazzoni:** I'm living more or less 60 kilometers away from the city where we had the
first outbreak of the virus, and actually, here, the schools were shut down three weeks
ago. At the beginning, not all of Italy was shut down, just this small part of Italy. I've been
in the epicenter for three weeks, and we saw the situation getting worse and worse
without any sign of relieving, up to the point where the state was forced to shut down
because we ran out of places in the hospital.

I can see the same dynamics all around the world. Probably, politicians fear taking too-
drastic measures, especially in the western world, and so they take one action after
another. But my experience is that all these actions do not really have effects, up until
the point where you have to force people to stay at home and shut down everything and
avoid people getting together, because this is a quite contagious virus, and just by
touching someone who has the virus you have a good chance of getting infected. So my
personal experience is that up to the shutdown, nothing has stopped the virus. We had
schools shut down for three weeks and we had not seen any sign of relief up to now
where we have shut down everything and now I think we will see the same dynamics.
Everyone is at home, we have only essential services running, so I think this will work.

**Snell:** It's been amazing to me how quickly things have been changing on a day-to-day
basis. Less than two weeks ago, I was live in Houston at the Rice Oil & Gas HPC
Conference, which is one of my favorite conferences of the year. It was in the middle of
the country, things seemed relatively stable – but by later in the week, when I was
supposed to be back here at home in San Jose for the Open Compute Project Summit,
that one was canceled. We're dealing of course with the cancellation of GTC [now GTC
Digital] and other, smaller events both in the United States and worldwide, with the cancellation of, for example, the supercomputing summit in Poland, the Dell HPC community event, the Cray User Group, the Women in HPC summit...

These all seem quite appropriate, now, in the context of much larger things going on: sporting events getting canceled, like the NBA and the NHL in the United States, the World Figure Skating Championships, Disneyland is closed, we’re now seeing a mobilization across the country of the cancellation of these larger-scale events. I don’t know how long it’ll be lasting, but this is our new normal for the time being.

**Cavazzoni:** Absolutely. We see the situation here in Italy as well, obviously, and we have seen all these steps already in the last month being taken here, closing one thing after another up to the complete shutdown. I’m confident that now the situation will start to improve in two weeks.

**Snell:** I’ve been speaking with Carlo Cavazzoni, senior staff member at Cineca. Carlo, thank you for joining me on the podcast, and more importantly, thank you for your very important work. I know and hope you’re very busy, and I’ll let you get back to it. Thanks for being with me this week in HPC.

**Cavazzoni:** Thank you, Addison, for the nice conversation.

**Snell:** Stay healthy everybody, wash your hands, and thanks for tuning in.

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