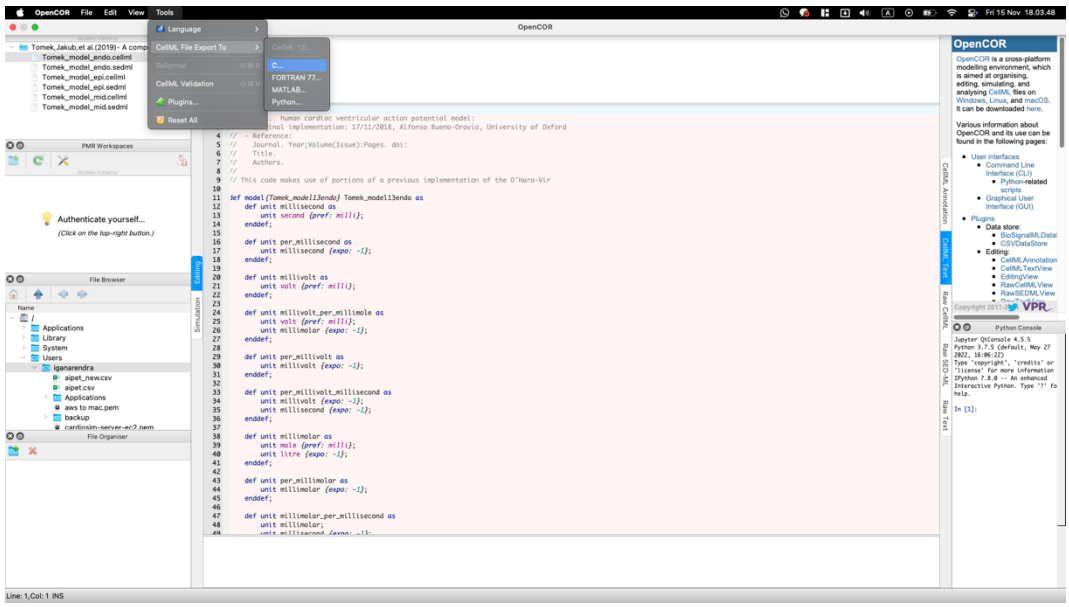
scripting, further enhance its utility for researchers. By leveraging OpenCOR, users can streamline the process of implementing CellML models into broader computational workflows, such as those involving high-performance computing or *in silico* drug testing.

This research involves three different cell models. O'Hara-Rudy 2011 [13], O'Hara-Rudy 2017 [14] and ToR-ORd [15]. After installing OpenCOR, open the application and search for these three cell models in the search bar on top left corner. Select file with .cellml extension. Select tools, and export the CellML file to C code. Figure 2.1 shows the OpenCOR GUI on MacOS.

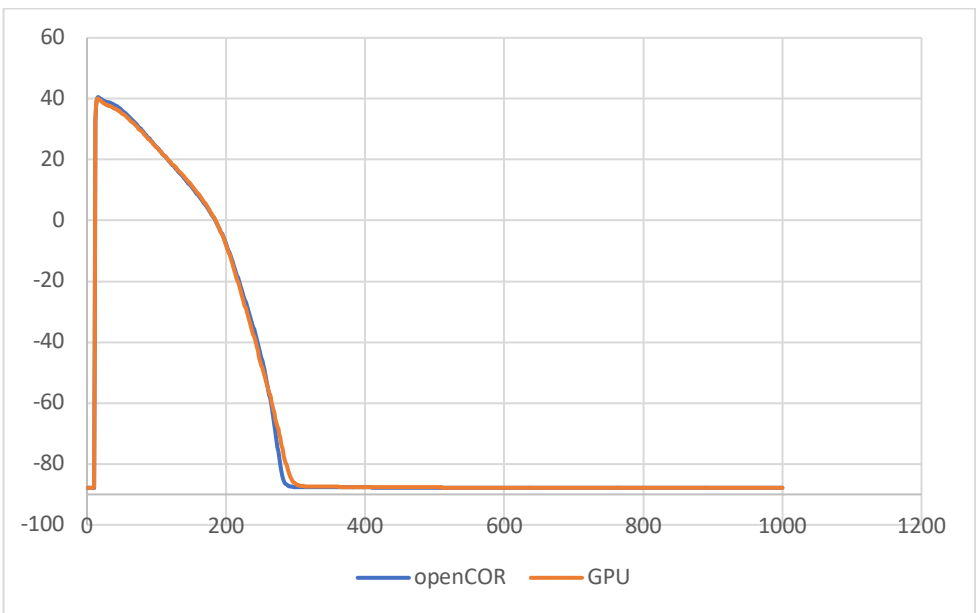


[Figure 2. 1] OpenCOR interface when selecting ToR-ORd model and converting it to C codes on MacOS.

Having the C code of the cell model is important because CUDA programming uses .cu format, that is similar to C. CUDA is built upon C/C++, extending it for GPU programming. Both use C syntax as their base language.

3.1.1 Result Validation

To validate the results of the GPU simulation, this research compared the action potential outputs against reference solutions obtained from the OpenCOR, running under CPU. Visual comparisons of time-series plots for action potentials were performed to ensure qualitative agreement. Key electrophysiological biomarker, such as action potential duration were also compared. These biomarkers from CPU and GPU were compared under a same, no drug conditions, ensuring that the GPU-based simulation accurately reproduces the physiological dynamics from the ORd 2011 model. The findings revealed the GPU simulation result is almost exactly same with its CPU predecessor. Figure 3.1 shows visually action potential from both simulation platforms.

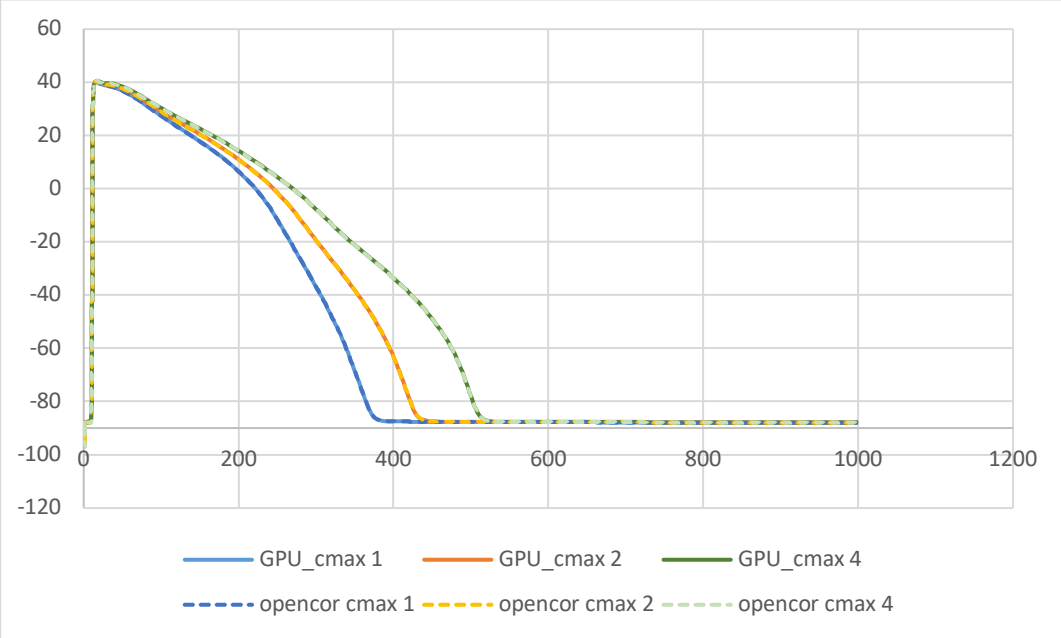


[Figure 3. 1] Action Potential (mV) Shape of both CPU (blue) and GPU (orange) Result Using ORd 2011

As shown, little to no difference from both of the result, indicating a valid result from the GPU-based simulation. Promising more efficient *in silico* drug cardiotoxicity prediction.

3.1.2 Result Validation Under Drug

This section evaluates the accuracy of the GPU-based simulation for the ORd 2011 cell model under drug conditions. Drug effects were modelled by adjusting ionic current parameters using IC50 and Hill coefficient values, applied consistently in both GPU and CPU (OpenCOR) simulations. Validation involved comparing action potential traces and key biomarker, such as action potential shape.

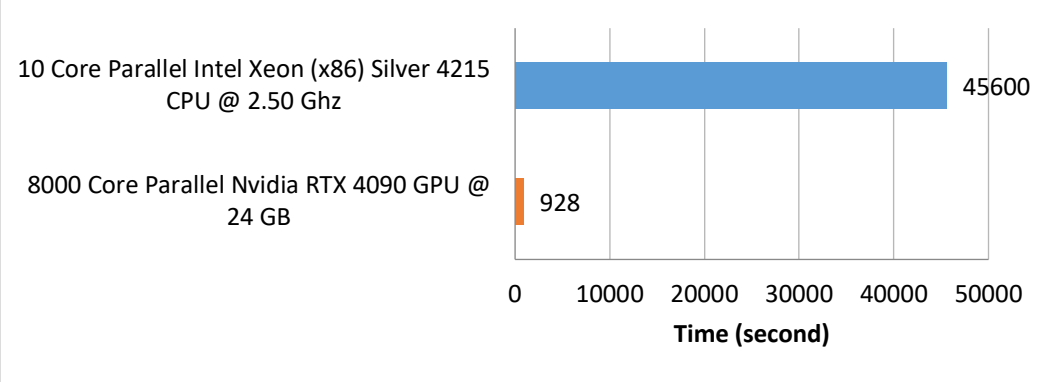


[Figure 3. 2] Action Potential Shape (mV) of both CPU (dashed) and GPU under drug effect Using ORd 2011

The results from figure 3.2 showed that despite the added complexity of drug effects, the GPU simulation closely matched the outputs of the CPU-based OpenCOR simulation. This confirms the GPU implementation's reliability in replicating physiological and pharmacological responses under drug conditions.

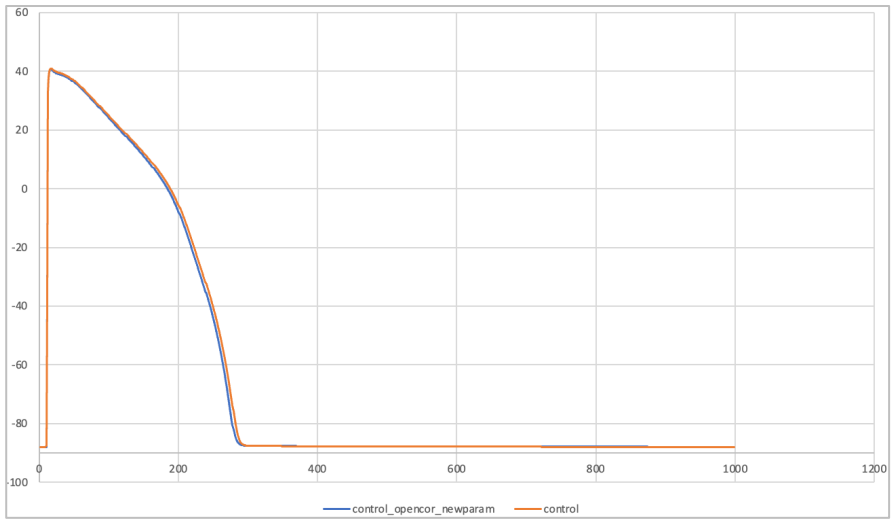
3.1.3 Computational Time and Efficiency Analysis

This analysis compares computational time between two hardware. GPU based simulation executed using NVIDIA RTX 4090 with 24 GB of memory. CPU based simulation also uses parallel processing of 10 cores Intel Xeon (x86) Silver 4215 CPU @ 2.50 GHz. The computational time compared for 8000 samples (each drug has 2000 samples, and 4 concentrations). In theory, GPU cores operate at lower clock speeds, making them inherently less powerful than CPU cores, which is why CPUs are typically preferred for single-sample simulations. The computation time for CPUs increases linearly with the sample size and pacing, meaning that as the number of samples grows, so does the time require for computation.



[Figure 3. 3] Simulation time comparison between GPU and CPU in ORd 2011

solutions generated from OpenCOR. Visual comparisons of action potential time-series data confirmed a close alignment between the two simulation platforms.

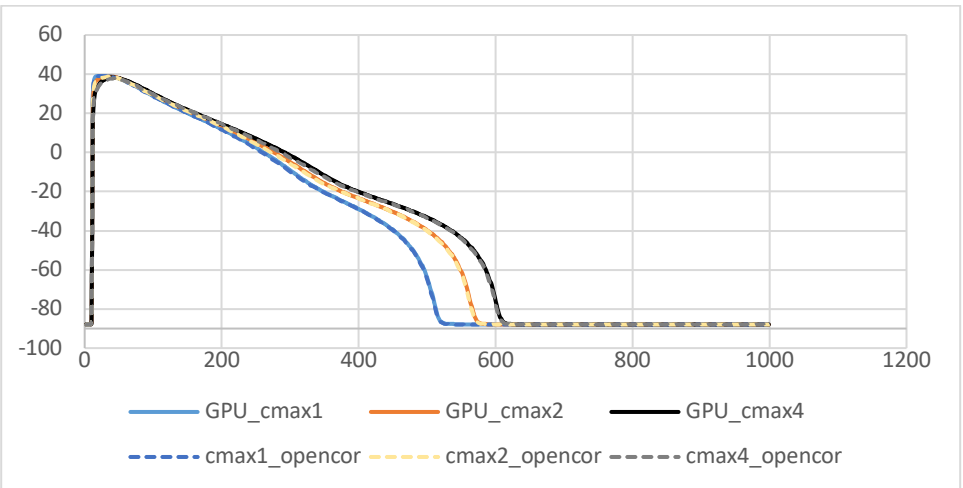


[Figure 3. 4] Action Potential (mV) Shape of both CPU (blue) and GPU (orange) Result Using ORd 2017

Key biomarker such as action potential duration, were analysed under identical no-drug conditions to ensure the physiological fidelity of the GPU-based results. As with the ORd 2011 model, the findings demonstrated that the GPU simulation similarly replicated the results from the CPU-based OpenCOR simulations. The numerical outputs showed no significant differences, confirming the reliability and accuracy of the GPU implementation for the ORd 2017 model. Figure 3.4 provides a visual comparison of the action potentials produced by the GPU and CPU simulations, illustrating their near-identical behaviour.

3.2.2 Result Validation Under Drug

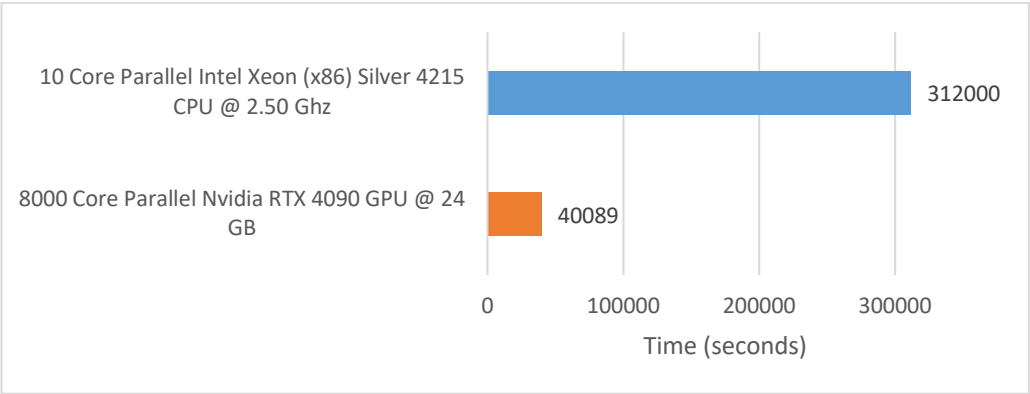
In this section, the accuracy of the GPU-based simulation for the ORd 2017 cell model was evaluated under drug conditions. The simulation incorporated drug-induced effects by modifying ionic current parameters based on IC50 and Hill coefficient values. These adjustments were applied uniformly across both the GPU and CPU (OpenCOR) simulations to ensure consistency in the drug response modelling. The validation process involved comparing action potential traces and key electrophysiological biomarker, such as action potential, between the GPU and CPU simulations.



[Figure 3. 5] Action Potential Shape (mV) of both CPU (dashed) and GPU under drug effect Using ORd 2017

Despite the added complexity of drug effects, the GPU simulation produced outputs that were nearly identical to those of the CPU-based OpenCOR simulations, as shown in figure 3.5. These findings confirm that the GPU implementation of the ORd 2017 model accurately captures the physiological and pharmacological responses of the cell model under drug conditions. This

(less than 40,089 seconds) would be faster than the GPU's fixed simulation time.



[Figure 3.6] Simulation time comparison between GPU and CPU in ORd 2017

For the ORd 2017 cell model, the GPU-based simulation achieved a speedup of up to 7.78 times compared to the 10-core CPU implementation. As shown in figure 3.6, GPU parallelisation is not as dominant compared to GPU parallelisation in ORd 2011. This lower speedup compared to the ORd 2011 cell model is attributed to the use of the Forward Euler method, which is computationally more demanding than the Rush-Larsen method. Nevertheless, the GPU remains significantly more efficient for large-scale simulations.

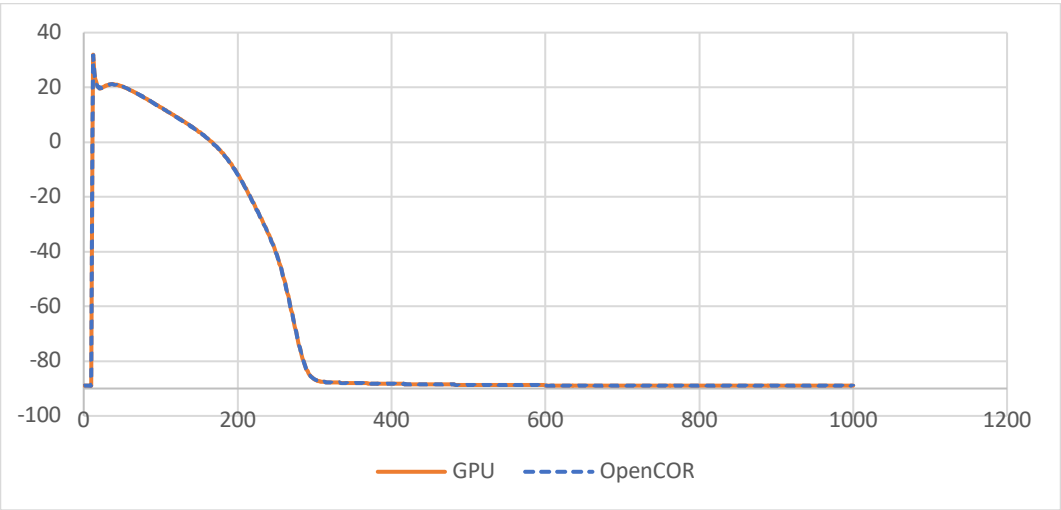
3.3 GPU Simulation Result Using ToR-ORd Cell Model

This section highlights the results obtained from GPU simulations using the ToR-ORd cell model. Similar to the ORd 2017 model, the forward Euler method was employed as the ODE solver. While this method provides adequate numerical stability and robustness for the ToR-ORD model, it results in longer computational times compared to the more efficient Rush-

Larsen method used in the ORd 2011 simulations. Regardless of the computational time drawback, forward Euler method ensure the simulation generates a reliable and usable result.

3.3.1 Result Validation

The validation process for the ToR-ORd cell model involved comparing GPU simulation outputs with the benchmark results obtained from OpenCOR. Time-series plots of action potentials were evaluated for qualitative consistency, and key biomarker, such as action potential duration, were quantitatively assessed under no-drug conditions.



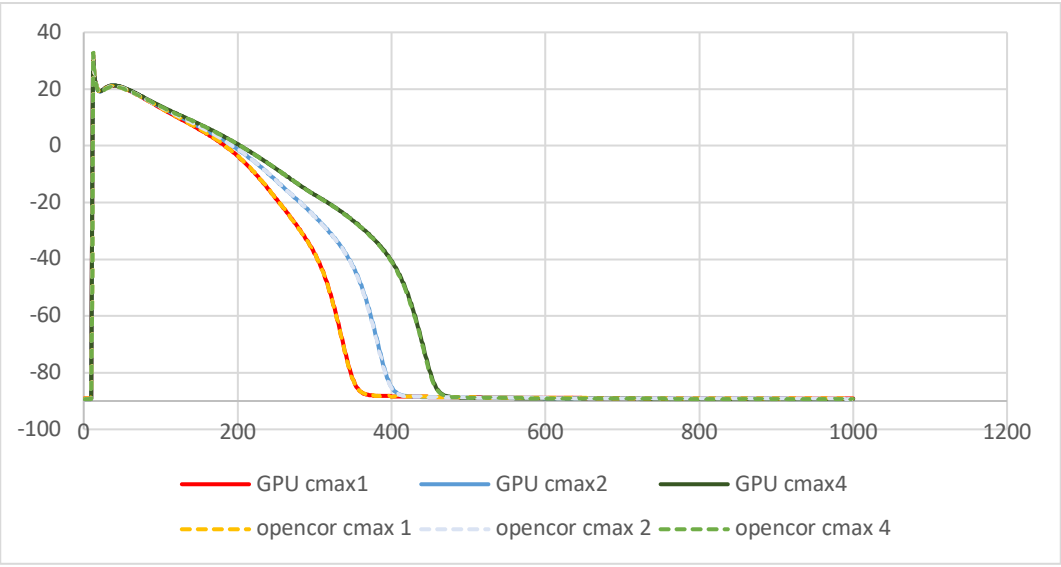
[Figure 3. 7] Action Potential (mV) Shape of both CPU (dashed blue) and GPU (orange) Result Using ToR-ORd

The results from figure 3.7 confirmed the accuracy of the GPU simulation, as it produced outputs that matched the CPU-based OpenCOR simulations without any discernible differences. This validation underscores the reliability of the GPU implementation for the ToR-ORd cell model, even

when employing the forward Euler method. Figure 3.6 illustrates the action potential traces from both GPU and CPU simulations, demonstrating their near-identical nature.

3.3.2 Result Validation Under Drug

For the validation in ToR-ORd cell model under drug, drug effects were incorporated into the simulation by altering ionic currents based on predefined IC50 and Hill coefficient parameters. Both GPU and CPU (OpenCOR) simulations were configured identically to ensure fair comparison.



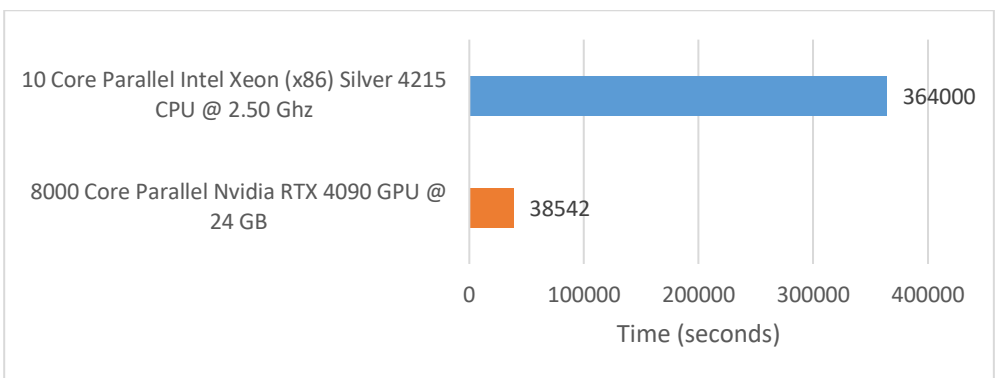
[Figure 3. 8] Action Potential (mV) Shape of both CPU (dashed) and GPU under drug effect Using ToR-ORd cell model

The results in figure 3. 8 showed that the GPU simulation accurately replicated the outputs of the CPU-based simulations, with no significant differences observed in action potential traces or in biomarkers such as APD, ionic current dynamics, and calcium handling. This consistency

demonstrates the validity of the GPU-based simulation for the ToR-ORd cell model, even when subjected to drug-induced perturbations. The successful validation of drug effects in the GPU simulations highlights the method's capability to simulate complex pharmacological scenarios reliably. These findings reinforce the utility of GPU-based simulations as a powerful tool for investigating drug-induced cellular behaviours.

3.3.3 Computational Time and Efficiency Analysis

The ToR-ORd cell model was also analysed using the same hardware: an NVIDIA RTX 4090 GPU and a 10-core Intel Xeon (x86) Silver 4215 CPU @ 2.50 GHz. The GPU executed the simulations for 8000 samples (2000 samples per drug at four concentrations), matching the experimental conditions of the CPU. Similar to the ORd 2017 cell model, the computational time for the ToR-ORd model on CPUs increased linearly with the number of samples and pacing due to sequential processing. In contrast, the GPU's architecture showed consistent computational performance, demonstrating parallelisation for large-scale simulations.



[Figure 3. 9] Simulation time comparison between GPU and CPU in ToR-ORd cell model