High-Performance Computing for Super-Resolution Microscopy on A Cluster of Computers

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Abstract—Multiple signal classification algorithm (MUSICAL) provides a super-resolution microscopy method. In the previous research, MUSICAL has enabled data-parallelism well on a desktop computer or a Linux-based server. However, the running time needs to be shorter. This paper will develop a new parallel MUSICAL with high efficiency and scalability on a cluster of computers. We achieve the purpose by using the optimal speed of the cluster cores, the latest parallel programming techniques, and the high-performance computing libraries, such as the Intel Threading Building Blocks (TBB), the Intel Math Kernel Library (MKL), and the unified parallel C++ (UPC++). Our experimental results show that the new parallel MUSICAL achieves a speed-up of 240.29x within 10 seconds on the 256-core cluster with an efficiency of 93.86%. Our MUSICAL offers a high possibility for real-life applications to make super-resolution microscopy within seconds.

Keywords—high-performance computing, computational nanoscopy, parallel programming, UPC++, super-resolution imaging.

I. INTRODUCTION

There are several techniques to overcome the Abbe diffraction limit to produce super-resolution microscopy. They include single-molecule localization microscopy (SMLM), photo-activated localization microscopy (PALM), structured illumination microscopy (SIM), and fluorescence fluctuations based super-resolution microscopy (FF-SRM). Azuma and Kei [1] presented a high-speed super-resolution confocal scanner based on its confocal scanner unit to obtain super-resolution microscopy. That research archived spatial resolution 100 nm and demonstrated temporal resolution 4.8 seconds for a cropped small stack image. Descloux et al. [2] used the SIM method to obtain super-resolution microscopy. In that research, the researchers demonstrated the performance of multiplane SIM and archived 74 time series of super-resolution SIM within 60 seconds. Hu et al. [3] used the SMLM technique to produce super-resolution microscopy. The researchers also used cloud computing for massive computing resources, i.e., the Amazon Elastic Compute Cloud (Amazon EC2). In that research, they demonstrated a super-resolution microscopy stack image 150x100x1500 in 210 minutes using Amazon EC2 300 instances of 600 virtual cores. Multiple signal classification algorithm (MUSICAL) [4] belongs to the family of FF-SRM. In research [5], researchers developed MUSICAL on a state-of-the-art desktop computer and a Linux-based server with a speed-up of 30.36x within 99 seconds and an efficiency of 94.88%.

The researchers in [5] planned to improve MUSICAL’s computational time using a cluster of computers or GPU. However, since each thread needs a large amount of high-speed memory, i.e., cache memory, a cluster of computers is more suitable. The researchers also proved that the Intel Threading Building Blocks (TBB) is better than other parallel techniques. The Intel Math Kernel Library (MKL) results in the best performance for large matrix multiplication. Hence, in this research, we apply TBB and MKL to the MUSICAL on a cluster of computers.

The performance of clusters of computers outperformed that of GPUs proved in the research in bioinformatics [6]. In that research, the unified parallel C++ (UPC++) resulted in high-performance computing enabling parallelism for a more significant number of cores in a cluster. In the research [6], UPC++ also exceeded the classical library such as Chapel in the Aries and InfiniBand systems.

We see some limitations in the given methods and results from the above review to produce high-speed super-resolution microscopy. Getting super-resolution microscopy, i.e., spatial resolution less than 100 nm, for a large input stack image, such as 2048x2048x500, took some minutes, which are too long for real-life applications. Time reduction is still a challenge because of past limitations in technologies, i.e., no parallel techniques and high-performance computing libraries, such as TBB, MKL, and UPC++, in [3][4], and limitations in resources, i.e., data-parallelism for super-resolution microscopy only on a single machine (no massive computing resources) in [5]. This paper presents a new parallel MUSICAL for a cluster of computers to solve the above limitations in technologies and resources and long execution time. Using the latest high-performance computing libraries, parallel programming techniques, i.e., TBB, MKL, and UPC++, we will minimize the time execution of the new MUSICAL on our cluster of computers.

The contributions of this paper are summarized as follows:

- We develop a new parallel MUSICAL in C++ for a cluster of computers using the latest high-performance computing libraries and parallel programming techniques, i.e., TBB, MKL, and UPC++.

- By using the optimal speed of the cluster cores, we achieve super-resolution microscopy with a speed-up of 240.29x within 10 seconds on a 256-core cluster with an efficiency of 93.86%.
• We provide a high possibility for real-life super-resolution microscopy applications within only 0.03 seconds, outperforming other methods in minutes, hours, or days.

II. NEW PARALLEL MUSICAL ON A CLUSTER OF COMPUTERS

A. MUSICAL Flowchart for A Cluster of Computers

In Do et al. [5], the researchers already described MUSICAL adapted from the research [4] for a desktop computer or a Linux-based server. In Fig. 1, we present another flowchart of MUSICAL for a cluster of computers.

![Flowchart of MUSICAL](image)

Fig. 1. The flowchart of the multiple signal classification algorithm (MUSICAL) for a cluster of computers. 3D = three-dimensional; CCD = charge-coupled device; ROI = region of interest; UPC++ = unified parallel C++.

In Fig. 1, we compute or load a point spread function (PSF) matrix in step 2. To reduce the program's running time, we put the following three steps outside loops for UPC++ parallel processing in nodes, multi-threading, and scanning window. Those steps are making a diagonal Gaussian mask in step 3, mapping a charge-coupled device (CCD) mask in step 4, and making a three-dimensional (3D) (x-y-z) stack image in step 5.

We choose one of two options for a manual threshold or calculating a singular value matrix and an auto-threshold value in step 6. Since we use multi-cores of multiple computers to speed up MUSICAL, the programming codes need to coordinate the work of all computers together. UPC++ developed by the Lawrence Berkeley National Laboratory is proper for this purpose. As proved in the research [7], UPC++ outperformed Chapel. Hence, we divide the 3D stack image into N horizontal partitions for UPC++ in step 7 and loop all nodes in step 8.

In each node, the input partitioned image is divided into M partitions for TBB’s multi-threading in step 9 and looped for all M partitions in step 10. Each pixel of one in M partitions is scanned and cropped into a 3D window in step 13. We calculate singular values and singular vectors for that window in step 14. Using the auto-threshold value in step 6, we determine the row positions in step 15. Using those positions, we divide singular vectors into the signal and the noise parts. We obtain ratios of the projections on the signal part of the input window and those on the noise part and take the power factor α to obtain a reconstructed window in step 16.

To get the same direction of the input window, we rotate 180 degrees for the reconstructed window in step 17. We collect all reconstructed windows into output the super-resolution image of M partitions inside a single node in step 18. After computing parallel processing for all N nodes, we stitch the final super-resolution image using `reduce_to_rank0` in step 19.

Compared with MUSICAL in a single machine, i.e., a desktop computer or a Linux-based server, MUSICAL in a cluster of computers must consider partitioning the input stack image to enable parallelism for multi-machines and each machine. We should also consider the optimal core speed. The following parts discuss parallel processing for nodes and the optimal number of cores per node.

B. Parallel Processing for Computational Nodes

Since UPC++ does not automatically partition the input stack image into smaller stack images for N nodes, we should consider partitioning the input stack image. We should also consider partitioning the smaller stack images into M partitions for TBB’s parallel process in each node.

Fig. 2 presents how we divide the input stack image into partitions for UPC++ in multi-nodes and multi-threading in each node. We have the input stack image in 3D. Then, we divide the input image into N horizontal partitions for N computational nodes for UPC++’s processing in step 7. We next divide each horizontal partition into M partitions for TBB’s multi-threading in step 9.

TBB was already applied successfully in the research [5]. In this research, we use UPC++ for parallel processing for multiple nodes. We send each partition in N partitions to each node and run a MUSICAL program with TBB similar to the program in research [5]. UPC++ executes the MUSICAL program on each node. However, collecting all partitions in a single machine in the research [5] is simple, but it is challenging in multi-nodes.
We summarize the stitching algorithm in step 19 presented in Algorithm I. We first create a global pointer on rank 0 to store all data from all nodes. Then, we broadcast the global pointer to all ranks. And then, we should point out a starting point for each node with a trunk equal to the amount of reconstructed data on each node. Next, we receive reconstructed data from each node and wait for all nodes returning the data to rank 0. Finally, we pass the data from the global pointer on rank 0 to the final reconstructed MUSICAL image.

C. Optimal Number of Cores Per Node

Our experimental cluster has three CPU types: Xeon Gold 6130, Xeon Gold 6126, and Xeon Gold 6138. We choose Xeon Gold 6138 [8] for our experiments since that CPU has the most significant number. In addition, since we have a quota for the maximum number of 256 cores, we should find the optimal combination of a number of cores per node and a number of nodes to get maximum speed-up for our MUSICAL program.

The memory for our MUSICAL program is mainly in the size of the PSF mapping matrix defined as follows:

\[ M = 4N_w^2Sub^2, \]  

where \( M \) is memory in byte for storing the PSF mapping matrix on the execution of each core; \( N_w \) is window size, ordinarily equal to 7; \( Sub \) is the subpixel per pixel factor to present how much super-resolution we want to have; factor 4 converts the matrix size in float to byte.

Our experiments used the Xeon Gold 6138 processor, which has a 27.5 MB cache for 20 cores, i.e., 1.375 MB cache for each core. Using Eq. (1), the memory for the PSF mapping matrix is 0.92 MB, 2.06 MB, and 3.66 MB for \( Sub \) of 10, 15, and 20, respectively. Hence, with the available high-speed cache
memory in the processor, we choose \textit{Sub} 10 for satisfying to maximize speed-up and scalability.

We have three available combinations of cores and nodes for a maximum quota of 256 cores. They are pairs of (nodes, cores): (8, 32), (16, 16), and (32, 8). Since our MUSICAL needs 32 GB memory per node, other pairs, (64, 4) with 16 GB memory per node and (128, 2) with 8 GB memory per node, cannot provide enough memory to run the MUSICAL program. However, variant frequencies are based on cores of the Intel Xeon 6138 [8], as shown in Table 1. In addition, our MUSICAL program includes large matrix multiplication for floating-point numbers; the CPU uses AVX512 mode. That means the CPU’s speeds for 32, 16, and 8 cores per node increase from 1.9, 2, and 2.7 GHz, respectively. The minimum number of cores per node returns the maximum frequency. Hence, we get the optimal speed-up for our MUSICAL if we choose 32 nodes and 8 cores per node.

III. EXPERIMENTAL RESULTS AND DISCUSSION

Experiments for this paper were undertaken on a shared cluster of computers with a maximum of 32 nodes and 256 cores. We used the Intel Xeon Gold 6138 CPU.

To evaluate of scalability, time, and image quality performance, we used two biomedical stack images, such as a cropped size of InVitroSample1.tif (150×100×1500) and several cropped sizes of 30.08.19-14.26.00.tif (2048×2048×500, 1536×1536×500, 1280×1280×500, and 1024×1024×500). We undertook three times with these stack images, recorded the average time results, calculated the speed-up, and indicated the error bars in all the following curves.

The optical parameters for InVitroSample1.tif were emission wavelength 510 nm, numerical aperture 1.49, magnification 100, pixel size 6500 nm, and window size 7. In addition, the optical parameters for 30.08.19-14.26.00.tif were emission wavelength 640 nm, numerical aperture 1.2, magnification 1, pixel size 108 nm, and window size 7. All stack images used the same MUSICAL parameters, such as turned-on auto-threshold option, alpha-factor 4, subpixels per pixel 10.

A. Evaluation for The Optimal Number of Cores Per Node

To have 256 cores per 32 nodes, we have three options: (8 nodes, 32 cores per node), (16 nodes, 16 cores per node), and (32 nodes, 8 cores per node). Section II.C has already shown variant frequencies based on the number of used cores of the Intel Xeon Gold 6138, where the minimum number of cores per node returns the maximum frequency. In this section, we prove this comment by our experimental results.

In this experiment, we use 30.08.19-14.26.00.tif 2048×2048×500 since the most significant size gives us the best scalability performance. That was proved in the research [5]. Other stack images have similar scalability, and we do not need to show results of all stack sizes.

Fig. 3 shows the performance of variable numbers of cores per node in running time and speed-up. The running times were measured from step 8 to step 20 in Fig. 1. Fig. 3a shows that we receive the best running time of 10 seconds with 8 cores per node compared with 16 cores per node and 32 cores per node for 12.33 s and 14.86 s, respectively.

We define a speed-up factor, \( S_{XY} \), of our MUSICAL on \( X \) cores compared with that on \( Y \) cores as follows:

\[
S_{XY} = \frac{T_Y}{T_X},
\]

where \( T_X \) and \( T_Y \) are the running times on \( X \) cores and \( Y \) cores, respectively. \( S_{XY} \) presents the factor with which the running time on \( Y \) cores performs faster than that on \( X \) cores.

Fig. 3b shows the speed-ups of different numbers of cores per node. Similar to the running time, 8 cores per node give the best speed-up performance of 240.29x (efficiency 93.86%) compared with 16 cores per node of 195.01x and 32 cores per node of 161.74x. The speed-up curves are perfect linearity since the running time was measured below \textit{upcxx\_barrier()}. That function synchronizes and waits for all nodes to finish the computation. Finally, we archive the best performance in running time and speed-up for using 8 cores per node on our cluster of computers with 32 nodes and 256 cores.

B. Reduce\_to\_rank0 Evaluation

We use 32 nodes with 256 cores to execute our MUSICAL program in our experiments. We use UPC++ developed by the Lawrence Berkeley National Laboratory to do that task. In step 7 of Fig. 1, we divide the input stack image into \( N \) horizontal partitions equal to the number of nodes \( (N=32) \). Then, MUSICAL can enable parallelism with those partitions. In each
node, UPC++’s partition is divided again into M partitions for TBB’s multithreading.

After running the whole MUSICAL process from step 8 to step 18, we stitch the reconstructed MUSICAL image in step 19 in Fig. 1. This means we take backward from c) to a) in Fig. 2. Stitching M partitions of TBB’s multi-threading is a simple step since that work is processed in a single machine and was taken in the research [5]. We discuss stitching for multiple nodes in this part.

There are two ways to stitch data from multiple nodes: saving to yml files or using Algorithm I in Section II.B. Using the way to save to yml files is a simple programming task, but the program consumes much, i.e., 28.82% of the total MUSICAL time. In contrast, Algorithm I uses only 2.58% of the total MUSICAL running time, shown in Fig. 4. Fig. 4 compares time consumption for stitching MUSICAL image using reduce_to_rank0 (Algorithm I) and saving to yml files for input image 2048×2048×500. Other image sizes have similar results.

![Time comparison for stitching multiple signal classification algorithm (MUSICAL) image.](image)

**C. Time and Scalability Evaluation**

To optimize scalability and parallelism of MUSICAL running on our cluster of computers, we took the following steps:

- **Big enough number of partitions:** We divided the input stack image into N partitions (equal to node numbers) for multi-node parallelism. Next, we divided each partition of the UPC++ process into 300-500 times the number of cores on each node for the TBB’s multithreading. We also added *shared-heap 2100M* for executing UPC++ with an enormous number of arrays (equal to the number of pixels) when stitching MUSICAL image as shown in Algorithm I.

- **Enough cache:** Using subpixels per pixel 10, we guarantee enough high-speed cache memory for MUSICAL parallelism as explained in Section II.C.

- **Optimal CPU speed:** Using 8 cores per node guarantees the best performance compared with other options, i.e., 16 cores per node and 32 cores per node as explained in Section II.C. Since we used shared multi-machines, we requested the memory as much as possible, i.e., mem-per-cpu = 4165M. To avoid other users using our machines, we tried to use the multi-machines before or after peak hours, for example, in the early morning. We also monitored the currently active users by *top* function.

By applying all the above steps, we obtain a running time performance of 10 seconds, core-based speed-up of 240.29x on 256 cores (efficiency 93.86%), and node-based speed-up of 31.69x on 32 nodes (efficiency 99.03%) for 2048×2048×500. Fig. 5 shows the performance of the other stack image sizes.

![Evaluation of time and scalability of multiple signal classification algorithm (MUSICAL) running on a cluster of computers.](image)
method [3] with 8 threads (9 days), Hu’s method [3] with 300 cloud threads (210 minutes), MUSICAL in MATLAB [4] with 8 threads (122.34 seconds), MUSICAL in C++ [5] with 32 threads (1.33 seconds), and our MUSICAL on our cluster of computers with 256 threads (0.03 seconds). Hence, our MUSICAL outperforms the other methods; it is faster than Hu’s method [3] up to 420,000x with a similar number of threads and the original MUSICAL [4] up to 4078x with 32 times the number of threads.

### TABLE II. COMPARISON OF TIME PERFORMANCE FOR IMAGE STACK OF SIZE 150x100x1500.

| Methods | Average time |
|---------|--------------|
| Hu’s method with 8 threads [3] | 9 days |
| Hu’s method with 300 threads [3] | 210 min. |
| MUSICAL in MATLAB with 8 threads [4] | 122.34 sec. |
| MUSICAL in C++ with 32 threads [5] | 1.33 sec. |
| Our MUSICAL on a cluster of computers with 256 threads | 0.03 sec. |

* The bold underlining represents the best performance.

### D. Image Quality Evaluation

We guarantee to keep the super-resolution image’s quality the same as the research [4][5]. However, the running time of our MUSICAL outperforms the others, as presented in the above section. We compare for 30.08.19-14.26.00.tif (160×160×500) cropped to get 1600×1600 and InVitroSample1.tif 150×100×1500 to get 1800×1500. Fig. 6 shows a similar image quality compared with the other MUSICAL programs in MATLAB, C++ on a single machine, and ours in C++ on our cluster of computers.

### IV. CONCLUSION AND FUTURE WORK

This paper has developed high-performance computing for super-resolution microscopy on a cluster of computers using the MUSICAL with parallel programming techniques and high-performance computing libraries, such as the Intel TBB and the Intel MKL, and the UPC++.

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