PARALLEL CALCULATION OF SUBGRAPH CENSUS IN BIOLOGICAL NETWORKS

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Abstract: Mining meaningful data from complex biological networks is a critical task in many areas of research. One important example is calculating the frequency of all subgraphs of a certain size, also known as the *subgraph census problem*. This can provide a very comprehensive structural characterization of a network and is also used as an intermediate step in the computation of network motifs, an important basic building block of networks, that try to bridge the gap between structure and function. The subgraph census problem is *computationally hard* and here we present several parallel strategies to solve this problem. Our initial strategies were refined towards achieving an efficient and scalable adaptive parallel algorithm. This algorithm achieves almost linear speedups up to 128 cores when applied to a representative set of biological networks from different domains and makes the calculation of census for larger subgraph sizes feasible.

1 INTRODUCTION

A broad range of biological structures can be represented as complex networks. The study of such networks is relatively recent and has received increased attention by the scientific community (Alm and Arkin, 2003). A large number of concepts and techniques appeared to analyze and understand complex networks from any domain, leading to an impressive panoply of different measurements used to mine interesting data from them (Costa et al., 2007).

One important measure is the frequency in which subgraphs appear in a network. Sometimes we are just interested in determining frequent patterns (Kuramochi and Karypis, 2001), while in others we need to determine a full count of all different classes of isomorphic subgraphs (Bordino et al., 2008). This last option is also known as a *subgraph census* and can provide a very accurate structural characterization of a network. This is typically applied for subgraphs of a specific size and it is normally limited to small sizes, mostly for efficiency reasons. This has been done not only on biological networks (Middendorf et al., 2004), but also on other domains, such as social networks analysis, where the triad census is very common (Wasserman et al., 1994).

Subgraph census also plays a major role as an intermediate step in the calculation of other important measures, such as *network motifs* (Milo et al., 2002), which are basically subgraphs that are statistically over-represented in the network (and conjectured to have some functional significance). Network motifs have applications on several biological domains, like protein-protein interaction (Albert and Albert, 2004), gene transcriptional regulation (Mazurie et al., 2005), brain networks (Sporns and Kotter, 2004) and food webs (Kondoh, 2008). Complex networks from other domains can also be studied with motifs, like electronic circuits (Itzkovitz et al., 2005) or software architecture (Valverde and Solé, 2005). The practical available algorithms and tools for network motifs all use a census to discover the frequency in the original network and then calculate it again for a series of similar randomized networks (Milo et al., 2002; Wernicke, 2006). This is a computationally hard problem that is closely related to the problem of graph isomorphism (McKay, 1981). Some techniques were developed to speedup the calculations, like sampling (Kashtan et al., 2004), but they normally trade accuracy for speed.

In all these applications, having a more efficient way to calculate the census is highly desirable. As we increase the size of the subgraphs, their frequency increases exponentially and it becomes unfeasible to count all of them using traditional approaches. Moreover, to date, almost all algorithms for complete sub-

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graph census are sequential. Some exceptions exist, particularly in the area of network motifs, but they are scarce and still limited (c.f. section 2.3). One reason is that present network motifs methods still resort to the generation of hundreds of random networks to measure significance. This puts the obvious opportunity for parallelism not in the census itself but in the generation of random networks and their respective census. However, analytical methods to estimate the significance are now appearing (Matias et al., 2006; Picard et al., 2008) and once they are fully developed the burden of the calculation will then reside on the census of the original network.

Considering the relevance of calculating exhaustive census and the computational complexity involved, resorting to parallel algorithms to speedup the calculation is, in our view, an approach that will impact in many application areas, particularly in the study of biological networks. The use of parallelism can not only speed up the calculation of census, but also allow the calculation of the census for subgraph sizes that were until now unreachable.

This paper focuses on strategies for solving the subgraph census problem in parallel. With this objective in mind we start with an efficient sequential algorithm, ESU (Wernicke, 2006), and progressively modify it to accommodate scalable parallel execution and data-structures. This process led us to the formulation of a novel adaptive parallel algorithm for subgraph census that features a work sharing scheme that dynamically adjusts to the available search-space. The results obtained show that the algorithm is efficient and scalable.

The remainder of this paper is organized as follows. Section 2 establishes a network terminology, formalizes the problem we want to tackle and gives an overview of related work. Section 3 details all the followed parallel strategies and the algorithm we developed. Section 4 discusses the results obtained when applied to a set of representative biological networks. Section 5 concludes the paper, commenting on the obtained results and suggesting possible future work.

2 PRELIMINARIES

2.1 Network Terminology

In order to have a well defined and coherent network terminology throughout the paper, we first review the main concepts and introduce some notation that will be used on the following sections.

A network can be modeled as a *graph* G composed of the set $V(G)$ of *vertices* or *nodes* and the set $E(G)$ of *edges* or *connections*. The *size* of a graph is the number of vertices and is written as $|V(G)|$. A k-graph is graph of size k. The *neighborhood* of a vertex $u \in V(G)$, denoted as $N(u)$, is composed by the set of vertices $v \in V(G)$ that are adjacent to u (u is not included). All vertices are assigned consecutive integer numbers starting from 0, and the comparison $v < u$ means that the index of v is lower than that of u.

A *subgraph* G_k of a graph G is a graph of size k in which $V(G_k) \subseteq V(G)$ and $E(G_k) \subseteq E(G)$. This subgraph is said to be *induced* if for any pair of vertices u and v of $V(G_k)$, (u,v) is an edge of G_k if and only if (u,v) is an edge of G. The neighborhood of a subgraph G_k, denoted by $N(G_k)$ is the union of $N(u)$ for all $u \in V(G_k)$. The *exclusive neighborhood* of a vertex u relative to a subgraph G_k is defined as $N_{excl}(u, G_k) = \{v \in N(u) : v \notin G_k \cup N(G_k)\}$.

A *mapping* of a graph is a bijection where each vertex is assigned a value. Two graphs G and H are said to be *isomorphic* if there is a one-to-one mapping between the vertices of both graphs where two vertices of G share an edge if and only if their corresponding vertices in H also share an edge.

2.2 Subgraph Census

We give a rigorous definition for the subgraph census problem:

Definition 1 (k-subgraph Census). *A k-subgraph census of a graph G is determined by the exact count of all occurrences of isomorphic induced subgraph classes of size k in G, where $k \leq |V(G)|$.*

Note that this definition is very broad and can be applied to all kinds of networks, whether they are directed or undirected, colored or not and weighted or unweighted. Also note that here, unlike in (Kashtan et al., 2004), we are concerned with an exact result and not just an approximation.

A crucial concept that we have not yet completely defined is how to distinguish two different occurrences of a subgraph. Given that we are only interested in finding induced subgraphs, we can allow an arbitrary overlap of vertices and edges or have some constraints such as no edge or vertex sharing by two occurrences. The several possibilities that we can have for the frequency are considered and discussed in (Schreiber and Schwobbermeyer, 2004). Here we focus on the most widely used definition that we formalize next:

Definition 2 (Different occurences of k-subgraphs). *Two occurrences of subgraphs of size k, in a graph G, are considered different if they have at least one vertex*

or edge that they do not share. All other vertices and edges can overlap.

Note that this has a vital importance on the number of subgraphs we find and consequently to the tractability of the problem.

2.3 Related Work

There exists a vast amount of work on graph mining. Particularly, the field of frequent subgraph mining has been very prolific, producing sequential algorithms like Gaston (Nijssen and Kok, 2004). Although related, these algorithms differ substantially in concept from our approach since their goal is to find the most frequent subgraphs that appear in a set of graphs, while we try to find the frequency of all subgraphs on a single graph.

Regarding subgraph census itself, most of the work on social networks is based on small sized subgraphs - mostly triads (Wasserman et al., 1994; Faust, 2007) - and therefore does not focus on efficiency, but rather on the interpretation of the results. However, for network motifs, efficiency does play an important role and much importance is given to the algorithm for generating the census. Increasing the speed may lead to detection of bigger patterns and even an increase in size of just one can yield scientifically important results because a new previously unseen pattern with functional significance may be discovered.

The three best known production tools for finding motifs are all based on serial algorithms. Mfinder (Milo et al., 2002) was the first and it is based on a recursive backtracking algorithm that generates all k-subgraphs. It may generate the same subgraph several times because it initiates a search procedure in each of its nodes. Fanmod (Wernicke, 2006) uses an improved algorithm called ESU, that only allows searches being initiated on the nodes with an index higher than the root node and therefore each subgraph is found only once. MAVisto (Schreiber and Schwobbermeyer, 2004) does not improve efficiency except when it uses a different concept for frequency.

Work on parallel algorithms for subgraph census is scarce. Wang and Parthasarathy (2004) propose an algorithm for finding frequent subgraphs but do not count all of them. Schatz et al. (2008) focuses on network motifs and how to parallelize queries of individual subgraphs and not on how to enumerate all of them.Wang et al. (2005) takes the closest approach to our work. Their algorithm relies on finding a neighborhood assignment for each node that avoids overlap and redundancy on subgraph counts, as in Wernicke (2006), and tries to statically balance the workload "a priori" based only on each node degree (no details are given on how this is done and how it scales). Another distinctive characteristic of their approach is that they do not do isomorphism tests during the parallel computation, they wait until the end to check all the subgraphs and compute the corresponding isomorphic classes. As we will see, our approach differs significantly from this one as it contributes with dynamic and adaptive strategies for load balancing, thus attaining higher efficiency.

3 PARALLEL ALGORITHMS

3.1 Core Sequential Unit

Given that we are interested in having an exact count of all classes of isomorphic subgraphs, we must enumerate all subgraphs. The ESU algorithm (Wernicke, 2006) is a key component of the fastest network motif tool available and as far as we know it is one of the most efficient algorithms for subgraph enumeration. Thus we chose the ESU algorithm as our starting point and modified its recursive part to create a procedure that given a graph G, a size k, a vertex minimum index min, a partially constructed subgraph $G_{subgraph}$, and a list of possible extension nodes V_{ext}, enumerates all k-subgraphs that contain $G_{subgraph}$ and no nodes with index lower than min. This procedure is depicted in algorithm 1. It recursively extends the subgraph $G_{subgraph}$ by first adding the new node u. If the new subgraph has size k, then it determines a unique identification and saves it in a dictionary. Otherwise, it expands the set of possible extension nodes, V_{ext}, with the nodes that are in the exclusive neighborhood of u relative to the subgraph $G_{subgraph}$ and also satisfy the property of being numerically bigger then min. If the extension set of nodes is not null then a new node is removed from extended V_{ext} and recursion is made.

Algorithm 1 Extending a partially enumerated subgraph.

```
1: procedure EXTEND(G, k, min, u, G_subgraph, V_ext)
2:     G'_subgraph ← G_subgraph ∪ {u}
3:     if |V(G'_subgraph)| = k then
4:         str ← CanonicalString(G'_subgraph)
5:         Dictionary.AddAndIncrement(str)
6:     else
7:         V'_ext ← V_ext ∪ {v ∈ N_excl(u, G_subgraph) : v > min}
8:         while V'_ext ≠ ∅ do
9:             Remove an arbitrarily chosen v ∈ V'_ext
10:            Extend(G, k, min, v, G'_subgraph, V'_ext)
```

Calling `Extend(` $G, k, u, u, \{\}, \{\}$`)` for every $u \in V(G)$ is exactly the equivalent to the original ESU algorithm. Therefore, as long as we call it on all nodes,

we can be certain that it will produce complete results, as shown in (Wernicke, 2006). Moreover, `Extend()` guarantees that each existent subgraph will only be found once on the call of its lowest index, as exemplified in figure 1. This avoids redundant calculations as in (Wang et al., 2005) and is crucial to achieve an efficient census.

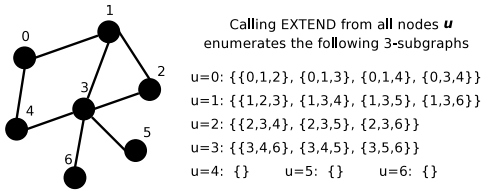


Figure 1: Example of how `Extend()` calls generate all subgraphs.

Before going into the details of the parallelism two additional notes are needed. First, isomorphism (line 4 of the procedure) is taken care of by using the canonical string representation of the graphs, defined as the concatenation of the elements of the adjacency matrix of the canonical labeling. In our case we use McKay's *nauty* algorithm (McKay, 1981), a widely known fast and practical implementation of isomorphism detection. Second, in order to store the results found within one call to our procedure (line 5), we use a string dictionary structure. This can be implemented in many ways, for example using an hash table or a balanced red-black tree. We implement the later (using STL *map* from C++).

3.2 Initial Parallel Approaches

Each of the aforementioned calls to `Extend(` $G,k,u,u,\{\},\{\}$ `)` is completely independent from each other and we call it a *primary* work unit. A possible way of parallelizing subgraph census is then to distribute these work units among all CPUs[1]. The problem is that these units have a computational cost with a huge variance, as the inherent substructure and the number of subgraphs each one enumerates are also quite different.

We experimented several strategies for the distribution in order to obtain the desired load balance. The first one was to statically allocate the units to workers before starting the census computation. In order to obtain good results this would need accurate estimates of the time that each unit takes to compute. We were unable to do that with the desired accuracy, since calculating this is almost as difficult as enumerating the subgraphs themselves.

We then took the path of a more dynamic approach using a master-worker architecture (Heymann et al., 2000). The master maintains a list of unprocessed primary work units. Workers ask the master for a unit, process it and repeat until there is nothing more to compute. Each worker maintains its own dictionary of frequencies. When all work units have been computed the master is responsible for collecting and merging all results, summing up the frequencies found.

The position of the work units on the master's list will determine the total time needed and we tried several strategies. Initially we just added all work units to the list in chronological order of the nodes. This proved to be a bad strategy since it is the same as a random assignment, which is in principle the worst possible (Heymann et al., 2000). We then experimented giving the work units sorted to an estimated cost, using *LPTF* (*Largest Processing Time First*) strategy. If the estimate was perfect, it is known that we would achieve at least $\frac{3}{4}$ of the optimum (Hall, 1997). We only had an approximation (based on the number of nodes achievable in $k-1$ steps) and therefore that boundary is not guaranteed. However, since our heuristic function maintained a reasonable ordering of the nodes, the performance was vastly improved.

We still had the problem that the call to a few primary work units (potentially even just one) could consume almost all the necessary compute time. This prevents good load balance strategies, given that each work units runs sequentially. This problems occurs very often in reality because typical complex networks are scale free (Barabasi and Albert, 1999). Whenever their hubs are the starting nodes of a work unit, very large neighborhoods are induced and a huge amount of subgraphs is generated. No matter what we do, there will always be a worker computing the largest sequential work unit and therefore the total compute time needed cannot be smaller than that. On some of our experiments with real biological networks, this largest atomic unit could consume more than 25% of the total execution time, which limits our scalability.

Considering that a work unit only calculates subgraphs containing nodes with indices greater than the index of the initial node, we devised a novel strategy in which we give higher index numbers to the potentially more time consuming nodes (those with larger degrees). We expected this to reduce the number of subgraphs spawning from these nodes, thus reducing the granularity of the work units induced by those

[1] from now on we will refer to processors in computational nodes as CPUs or workers to avoid confusion between them and graph nodes.

nodes. To accomplish this strategy, we implemented a node relabeling algorithm in which the nodes are sorted increasingly by their degree. Figure 2 gives a practical example of this strategy at work, producing a more balanced graph.

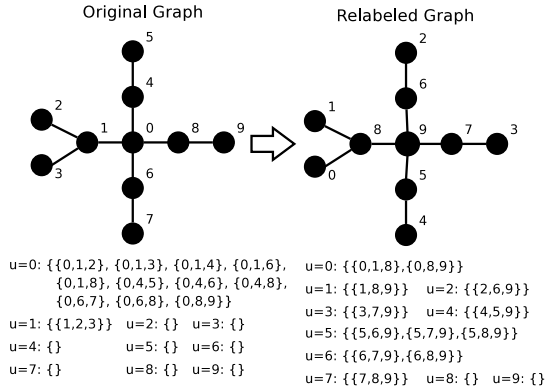
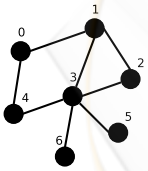


Figure 2: Relabeling the graph to balance primary work units.

Although this last approach improved our results, we expected that for some networks the relabeling strategy could not reduce enough the granularity of the work units, thus preventing scalability. We felt that we really needed a strategy that could divide the work units further.

3.3 Adaptive Parallel Enumeration

By inspecting the computation flow of a primary work unit, we can observe that there are several recursive calls to `Extend()` , as exemplified in figure 3 (for simplicity, we do not show G and k since these are fixed arguments).

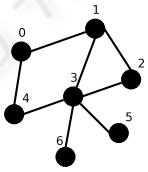


`Extend(` 0, 0, {}, {}`)`
$V'_{ext} = \{1,4\}$
`Extend(` 0, 1, {0}, {4}`)`
$V'_{ext} = \{2,3,4\}$
`Extend(` 0, 2, {0,1}, {3,4}`)`
→ Found subgraph $\{0,1,2\}$
`Extend(` 0, 3, {0,1}, {4}`)`
→ Found subgraph $\{0,1,3\}$
`Extend(` 0, 4, {0,1}, {}`)`
→ Found subgraph $0,1,4$
`Extend(` 0, 4, {0}, {}`)`
$V'_{ext} = \{3\}$
`Extend(` 0, 3, {0,4}, {}`)`
→ Found subgraph $0,3,4$

Figure 3: The computation flow of a primary work unit.

With our formulation of `Extend()` , all recursive calls are independent with no need for information of previous data on the recursion stack besides the arguments it was called with. One way to divide a primary work unit is therefore to partitionate it in its recursive calls. A tuple $(min, u, G_{subgraph}, V_{ext})$ completely defines the resulting call to `Extend()` and we will now call work unit to a tuple like this, with primary work units being only a particular case.

Our new strategy to reduce the granularity of the work units uses a threshold parameter to indicate the point in the computation at which we split the execution of the current work unit into smaller work units. Instead of really computing subsequent recursive calls, we encapsulate their arguments into new smaller work units and send them to the master to be added to the list of unprocessed work, effectively dividing our previously atomic sequential units. This leads to a simpler, yet elegant, solution when compared to more common adaptive strategies that need a queue in each computation node (Eager et al., 1986). Figure 4 illustrates our strategy at work. Remember that the new work units are still independent and we do not need to be concerned with locality. All subgraphs will be found and added to the respective worker's dictionary of frequencies, being merged in the end of the whole computation to determine the global resulting census.



`Extend(` 0, 0, {}, {}`)`
$V'_{ext} = \{1,4\}$
`Extend(` 0, 1, {0}, {4}`)`
$V'_{ext} = \{2,3,4\}$
`Extend(` 0, 2, {0,1}, {3,4}`)`
→ Found subgraph $\{0,1,2\}$
——— Splitting Threshold ———
`Extend(` 0, 3, {0,1}, {4}`)`
⇒ New work unit with these arguments
`Extend(` 0, 4, {0,1}, {}`)`
⇒ New work unit with these arguments
`Extend(` 0, 4, {0}, {}`)`
⇒ New work unit with these arguments

Figure 4: Work split strategy for work units.

Our algorithm is able to adjust itself during execution using this division strategy. It splits large work units into new smaller work units ensuring that their grain-size will never be larger than the size of work units executed up to the threshold value. In doing so, we are able to improve the load balancing and thus achieve an effective dynamic and adaptive behavior.

The splitting threshold parameter is central in our adaptive algorithm. If it is set too high, the work units will not be sufficiently divided in order to adequately balance the work among all CPUs. If it is too low, work will be divided too soon and the communication costs will increase. As a proof of concept our cur-

rent implementation uses a threshold that limits the computation time spent on a work unit to a maximum value, but other measures could be used like for example the number of subgraphs already enumerated.

One aspect not yet discussed, but that is orthogonal to all discussed strategies, concerns the aggregation of results at the master. If a naive approach was taken, then each worker would be sending their results to the master sequentially. This would be highly inefficient and therefore we devised a parallel approach for this final step. We use an hierarchical binary tree to organize the aggregation of results, where each worker receives the results of two other *child* workers, updates its own frequency dictionary accordingly, and then in turn sends the aggregated results to its parent. This is exemplified in figure 5 and has the potential to logarithmically reduce the total time needed to accomplish this step.

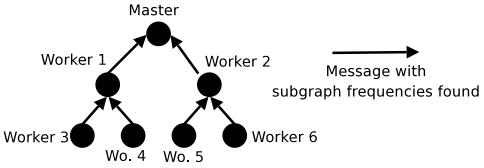


Figure 5: Example of results aggregation with 1 master and 6 workers.

All the ideas described are the basis for our main algorithm that we called *Adaptive Parallel Enumeration* (APE). Algorithms 2 and 3 describe in detail our APE master and worker procedures.

Algorithm 2 APE master node.

```
 1: procedure MASTER(G,k)
 2:     L_WorkUnits.add(AllPrimaryWorkUnits)
 3:     while CPUsWorking ≠ ∅ do
 4:         msg ← ReceiveMessage(AnyWorker)
 5:         if msg.type = RequestForWork then
 6:             if L_WorkUnits.notEmpty() then
 7:                 W ← L_WorkUnits.pop()
 8:                 newMsg ← EncapsulateWorkUnit(W)
 9:                 SendMessage(msg.Sender, newMsg)
10:             else
11:                 IdleWorkers.push(msg.Sender)
12:         else if msg.type = NewWorkUnit then
13:             if IdleWorkers.notEmpty() then
14:                 worker ← IdleWorker.pop()
15:                 SendMessage(worker, msg)
16:             else
17:                 W ← ExtractWorkUnit(msg)
18:                 L_WorkUnits.push(W)
19:     BroadcastMessage(Terminate);
20:     ReceiveResults(LeftChild, RightChild)
```

The master starts by adding all primary work units to the list of unprocessed work units ($L_{WorkUnits}$). Then starts its main cycle where it waits for a message from a worker. If the message indicates that the worker needs more work, the master sends it the next unprocessed work unit $L_{WorkUnits}$. If the list is empty, the master signals the worker as being idle. If the message indicates that the worker is splitting work and thus sending a new unprocessed work unit, then the master adds that new work unit to $L_{WorkUnits}$. If there is an idle worker, then this unit is sent right away to that worker. When all workers are idle, the subgraph enumeration is complete and the master ends its main cycle, broadcasting to all workers that event. What remains is then to collect the results and following the explained hierarchical aggregation process, the master receives the results of two workers and merges them in an unified global dictionary of the frequencies of each isomorphic class of k-subgraphs.

Algorithm 3 APE worker node.

```
 1: procedure WORKER(G,k)
 2:     while msg.type ≠ Terminate do
 3:         msg ← ReceiveMessage(Master)
 4:         if msg.type = NewWorkUnit then
 5:             W = (G,k,min,u,G_subgraph,V_ext) ← ExtractWorkUnit(msg)
 6:             Extend'(W)
 7:     ReceiveResults(LeftChild, RightChild)
 8:     SendResults(ParentWorker)

 9: procedure EXTEND'(W)
10:     if SplittingThresholdAchieved() then
11:         msg ← EncapsulateWorkUnit(W)
12:         SendMessage(Master, msg)
13:     else
14:         lines 2 to 9 of algorithm 1
15:         Extend'(W' = (G,k,min,v,G'_subgraph,V'_ext))
16:         lines 11 and 12 of algorithm 1
```

The worker has a main cycle where it waits for messages from the master. If the message signals a new work unit to be processed, than it calls a modified version of the `Extend()` procedure to compute that work unit. If the message signals termination, then it exits the cycle, receiving and merging the results from two other workers with its own dictionary. It then send those results to a single parent processor, that depending on the worker rank number may be other worker or the master itself, completing the hierarchical aggregation phase. Regarding the modified version of the `Extend()` procedure, it is exactly the same as the version depicted on algorithm 1 except the fact than when the splitting threshold is achieved, the computation is stopped and all subsequent calls consist now in encapsulating the arguments into a new work unit and sending it to the master.

There are two issues that we would like to clarify.

Table 1: Networks used for experimental testing of the algorithms.

Network	Nodes	Edges	Avg. Degree	Description
Neural	297	2345	7.90	Neural network of *C. elegans*
Gene	688	1079	1.57	Gene regulation network of *S. cerevisiae*
Metabolic	1057	2527	2.39	Metabolic network of *S. pneumoniae*
Protein	2361	7182	3.04	Protein-protein interaction network of *S. cerevisiae*

First, we decided to use a dedicated master because it is a central piece in the architecture and we needed the highest possible throughput in the assignment of new work units to idle workers. Second, APE was originally created having in mind homogeneous resources but its dynamic and adaptive design makes it also suited for heterogeneous environments.

Table 2: Maximum achievable subgraph sizes k using a serial program.

Network	k	Time spent (s)	Average Growth	Total nr of subgraphs	Isomor. classes
Neural	6	10,982.9	47.6±0.4	1.3×10^{10}	286,376
Gene	7	4,951.0	19.0±1.4	4.2×10^{9}	4,089
Metabolic	6	14,000.1	46.5±2.7	1.9×10^{10}	1,696
Protein	6	10,055.2	31.2±3.1	1.3×10^{10}	231,620

4 RESULTS

All experimental results were obtained on a dedicated cluster with 12 SuperMicro Twinview Servers for a total of 24 nodes. Each node has 2 quad core Xeon 5335 processors and 12 GB of RAM, totaling 192 cores, 288 GB of RAM, and 3.8TB of disk space, using Infiniband interconnect. The code was developed in C++ and compiled with gcc 4.1.2. For message passing we used OpenMPI 1.2.7. All the times measured were *wall clock times* meaning real time from the start to the end of all processes.

In order to evaluate our parallel algorithms we used four different representative biological networks from different domains: Neural (Watts and Strogatz, 1998), Gene (Milo et al., 2002), Metabolic (Jeong et al., 2000) and Protein (Bu et al., 2003). The networks present varied topological features that are summarized in Table 1.

We first studied the computational behaviour of each network using the equivalent to the ESU algorithm, sequentially calling all primary work units (with no MPI overhead). This measures how much time a serial program would take to calculate a subgraph census. We took note of what was the maximum possible subgraph size k achievable in a reasonable amount of time (we chose one hour as the maximum time limit). We calculated the average growth ratio, that is, by which factor did the execution time grew up as we increased k by one. Finally, we also calculated the total number of different occurrences of k-subgraphs and the number of different classes of isomorphism found on those subgraphs. The results obtained can be seen in table 2.

Note the relatively small subgraph sizes achievable. This is not caused by our implementation, since using the FANMOD tool (Wernicke, 2006), the fastest available for network motifs calculation, we also were only able to achieve the same maximum k in one hour. The cause is that, as expected, the computing time grows exponentially as the subgraph size increases. We also observe that although different graphs present very different average growths, the growth rate for a given graph seems fairly constant (note the standard deviation).

For the next set of results we decided to fix the respective k for each graph to the values depicted in table 2, in order to have more comparable results. We evaluated the parallel strategies described in section 3. We compared the speedup obtained on all three graphs for the dynamic strategy with chronological order in the work units list (DYN-CRON), with LPTF ordering (DYN-LPTF), with graph relabeling followed by LPTF (DYN-RELABEL) and finally with the APE strategy.

For the APE algorithm it is necessary to explain how we chose the value for the splitting threshold parameter. We chose to employ the time spent in the same work unit as a proof of concept for the usefulness of APE and we empirically experimented several values for this time limit, reducing it while verifying that the speedup was being improved. This value controls the granularity of the work units. We want it as small as possible, as long as the increase in communication costs does not overcome the effect of increased sharing. We found that for our context 2 seconds appeared to be a good and balanced value (the time spent in communications during the enumeration of the subgraphs was always smaller than 2% of the total time spent), and we measured the speedup with that particular value chosen as the threshold (APE-2s).

We used a minimum of 8 CPUs because each computation node in the cluster had precisely that number of processors. With less CPUs the nodes would not

Table 3: Detailed APE behavior with splitting threshold set to 2s.

Network	k	#CPUs: speedup (% time spent in aggregating results)				
		8	16	32	64	128
Neural	6	7.0 (0.2%)	14.8 (1.2%)	30.1 (3.4%)	58.7 (8.0%)	107.0 (16.9%)
Gene	7	7.0 (0.1%)	15.0 (0.2%)	30.7 (0.4%)	62.0 (0.8%)	125.0 (0.7%)
Metabolic	6	6.9 (0.1%)	14.9 (0.1%)	30.8 (0.3%)	62.4 (0.6%)	125.5 (1.3%)
Protein	6	6.6 (0.2%)	13.7 (1.2%)	28.0 (3.3%)	54.6 (7.4%)	96.9 (18.8%)

be exclusively dedicated to the subgraph census. The results obtained up to 128 processors are depicted in figure 6. The results obtained clearly show different performance levels for the different strategies. Generally speaking, the strategies based on the atomic primary work units do not scale well, although the incremental strategies used show some improvements in the speedup. Overall, as expected, the adaptive strategy, APE-2s, outperforms all others and clearly achieves scalability.

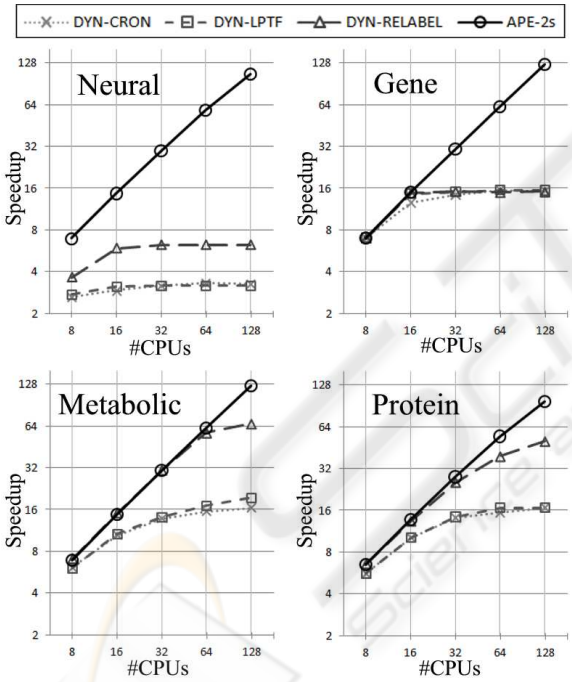


Figure 6: Speedups obtained with several parallel approaches.

Next, we further analyze the performance of APE-2s on all networks. Table 3 details the performance of the APE-2s up to 128 processors, and show the percentage of time spent in the final step of aggregating all frequency results in the master CPU.

We can observe that for Gene and Metabolic , APE-2s obtains almost perfect linear speedup, with a reduced amount of time spent in the aggregation phase. In Neural and Protein , despite the good results, there is still some room for improvement. The time spent communicating the results in the end of the computation, more than 15% of the execution time with 128 processors, is the cause for the loss in the speedup. In fact, with more than 200,000 classes of isomorphic subgraphs in the network (see table 2), each worker has to communicate all of the frequencies it finds in its respective computation. On average, the number of different classes of isomorphism discovered on the same CPU, is larger than 150,000. Each of these classes has to be encapsulated (uniquely identifying the class) in order for the receiver to be able to decode it and merge the results. Even with our hierarchical method for aggregating the results, this still takes a considerable amount of time. This effect is not so noticeable in the other networks since the number of different classes found is much lower (due to inherent network topology, with a smaller average degree per node).

As a final demonstration of the relevance of our algorithm, consider the average growth as we increase k (shown in Table 2). As long as the number of processors we have available is larger than the average growth, we should be able to compute the $(k+1)$-census in the same amount of time we initially were able to compute the k-census sequentially. For example, using the average growth, we can estimate that calculating a 7-census of Metabolic would take more than one week, if done sequentially. Using 128 processors and APE-2s, we were able to calculate it in less than 1h30m, spending even less than half of the time a sequential 6-census takes.

5 CONCLUSIONS

We presented several strategies for calculating subgraph census of biological networks in parallel. Our approaches are based on an efficient sequential algorithm called ESU that we parallelized by initially modifying it to a version capable of producing independent and dividable work units. We started with a dynamic master-worker strategy and subsequently improved it with an LPTF order of processing and a smart relabeling of the nodes in the graph. We also

presented APE, a novel adaptive load balancing algorithm, which includes an hierarchical aggregation of the results found in each worker. APE proved to be an acceptable and scalable solution for the set of representative networks studied, successfully reducing the time needed to calculate the subgraph census and achieving larger subgraph sizes than were before possible.

The main drawback of APE seems to be the final aggregation of results. We plan to research and improve this step in the future. One way of doing it would be to use a more compact and compressed representation of the results. We also plan to research the splitting threshold parameter in order to better understand on what does it depend, exactly how does it affect the computation and how could it be automatically determined by the algorithm. We are collaborating with neuroinformatics scientists in order to apply the described strategies on real neural networks to obtain new and interesting results on previously unfeasible subgraph census.

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