Simulation scalability of large brain neuronal networks thanks to time asynchrony

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We present here a new algorithm based on a random model for sim-1

ulating efficiently large brain neuronal networks. Model parameters 2 (mean firing rate, number of neurons, synaptic connection probabil-

3 ity and postsynaptic duration) are easy to calibrate further on real

data experiments. Based on time asynchrony assumption, both com-

5 putational and memory complexities are proved to be theoretically

6 linear with the number of neurons. These results are experimen-

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tally validated by sequential simulations of millions of neurons and 8 billions of synapses in few minutes on a single processor desktop

computer. 10

> Brain neuronal networks | Random models | Point processes | Stochastic simulation | Discrete event systems | Time asynchrony | Hawkes processes.

here are more and more vast research projects, whose 1 aim is to simulate brain areas or even complete brains 2 to better understand the way it works. Let us cite for in-3 stance: the Human Brain Project (1) in Europe, the Brain 4 Mapping by Integrated Neurotechnologies for Disease Studies 5 (Brain/MINDS) (2) in Japan or the Brain Initiative (3) in 6 the United-States. Several approaches are feasible. There is 7 the biochemical approach (4), which is doomed for systems 8 as complex as the brain. A more biophysical approach has 9 been investigated, see for instance (5), where cortical barrels 10 have been successfully simulated, but are limited to about 10^5 11 neurons. However, the human brain contains about 10^{11} neu-12 rons whereas a small monkey, like marmosets (2), has already 13 6×10^8 neurons (6) and a bigger monkey, like a macaque, has 14 6×10^9 neurons (6). 15

To simulate such huge networks, models reduction have 16 to be made. In particular, a neuron has no more physical 17 shape and is just represented by a point in a network with 18 a certain voltage. Hodgkin-Huxley equations (7) are able 19 to reproduce the physical shape if it is combined to other 20 differential equations, representing the dynamic of ion channels, 21 but the complexity of these coupled equations that form a 22 chaotic system (8), makes the system quite difficult to simulate 23 for huge networks. If ion channels dynamic is neglected, the 24 simplest model of voltage is the Integrate-and-Fire model (9). 25 With such models, it has been possible on supercomputers 26 to simulate a human-scale cerebellar network reaching about 27 68×10^9 neurons (10). 28

However there is another point of view, which might allow 29 us to simulate such massive networks with simplified models. 30 Indeed, one can use much more random models to reproduce 31 the essential dynamics of the neurons: their firing pattern. 32 The randomization of not only the connectivity graph but also 33 the dynamics on the graph is making the model closer to the 34 data at hand and explain to a certain extent their variability. 35 The introduction of randomness is not new and has been done 36 in many models including Hodgkin-Huxley (11) and Leaky 37

Integrate-and-fire (LIF for short) (12).

Here we want to focus on particular random models - point processes (13) - which have a particular property: time asynchrony, that is the inability of the model to have two spikes that are produced exactly at the same time by two different neurons. This includes in particular Hawkes models and variants such as GLM, Wold processes, Galves-Löcherbach models, and even some random LIF models with random or soft threshold, all of them having been used to fit real data (13-19).

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This property, which is well known in mathematics (14,20), combined with graph sparsity lead us to propose a new algorithm in (21). The computational complexity of this new algorithm has been computed. Thanks to time asynchrony and to the computational activity tracking of firing neurons (22), we have shown in particular that if the graph is sparse, the complexity cost of the computation of a new point in the system is linear in the number of neurons. However the memory burden was too high to reach networks of 10⁸ neurons.

In a preliminary work (23) focusing on the mathematical 57 aspects of mean-field limits of LIFs, we formalized a way to 58 deal with this memory aspect without putting it into practice: 59 the main point is to not keep in memory the whole network, 60 but to regenerate it when need be. Recently, the same idea, 61 under the name of procedural connectivity, has been applied 62 with success on LIF models in (24): using GPU-based parallel 63 programming, and without time asynchrony, the authors have 64 been able to simulate a network of 4×10^6 neurons and 24×10^9 65 synapses on a desktop GPU computer. 66

But, as we show in the present article, the gain of procedural connectivity is even huger when combined with time

Significance Statement

Time asynchrony refers to models that prevent any two neurons to fire at the exact same time (up to the numerical precision). Brain models that are time asynchronous have a huge numerical advantage on other ones: they can be easily simulated without huge parallelization or use of GPU. Indeed, this work proposes to exploit the time asynchrony property to derive new simulation algorithms, whose computational and memory complexity can be estimated beforehand. Application on realistic set of parameters show that they can indeed easily reach the size of a small monkey brain, on a usual single processor desktop computer.

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asynchrony. Indeed, classical parallel programming usually 69 uses a discrete simulation time and computes for all neurons 70 (or synapses) what happens at each time step in a parallel 71 fashion (even if spikes can be communicated in between two 72 73 time steps (10)). At each time step, each process correspond-74 ing to a different neuron has to wait for the calculations of all the other processes to know what needs to be updated 75 before computing the next step. With time asynchrony, we 76 can leverage discrete-event programming (25-28) to track the 77 whole system in time by jumps: from one spike in the net-78 work to another spike in the network. Since a very small 79 percentage of a brain is firing during a given unit of time 80 (29), the gain we have is tremendous in terms of computations. 81 Thanks to the procedural connectivity, the memory needed 82 to access for the computation of each new spike is also con-83 trolled. Hence, thanks to procedural connectivity combined 84 with time asynchrony, we propose a new algorithm for time 85 asynchronous models, running sequentially on a single pro-86 cessor, thus simulating a realistic network of 10^8 neurons for 87 which computational complexity as well as memory costs can 88 be controlled beforehand. 89

Results 90

Time synchrony for parallel simulation. Brain simulation of 91 large networks is usually done in parallel based on simulation 92 synchronization. Of course, this depends on both the mathe-93 matical model at hand and the simulation algorithm. However, 94 for most models, differential equations are used to derive the 95 time course of the membrane voltage for each individual neu-96 rons. These equations are (approximately) solved by usual 97 98 discrete-time numerical schemes (cf. Figure 1a) (24). 99 In this kind of implementation, when one presynaptic neu-

ron fires at a time t, *i.e.*, emits a spike (red dots in Figure 100 1a), the synaptic transmission to post-synaptic neurons is 101 done at the next time step $t + \Delta t$ (orange dots in Figure 1a). 102 Between two synaptic transmissions, the membrane potential 103 of a neuron evolves independently of the other neurons and 104 can be computed in parallel (green dots in Figure 1a). How-105 ever, since one does not know when a spike will be emitted 106 107 in the network in advance, the membrane potential of all the neurons are classically computed in a synchronous way to be 108 able to eventually transmit spikes, at each time step Δt of the 109 algorithm. 110

Time asynchrony for sequential simulation. As said in the in-111 troduction, point processes models of neuronal network may 112 guarantee time asynchrony if they have a stochastic intensity. 113 Such processes include Hawkes processes, GLM approaches, 114 Wold processes or Galvès Löcherbach models in continuous 115 time (13, 15-18). Most of these models have proved their 116 efficiency in terms of goodness-of-fit with respect to real spike 117 train data (13-17, 30). Often, the intensity in these models 118 can be informally interpreted as a function of the membrane 119 voltage and for more evidence, we refer the reader to (31), 120 where the spike train of a motor neuron has been shown to 121 be adequately modeled by a point process whose stochastic 122 intensity is a function of the membrane voltage. 123

These point processes models differ from classical LIF, 124 mainly because the higher the intensity (or the membrane 125 potential) of a given neuron is, the more likely it is that the 126 neuron fires, but this is never for sure. In classical LIF models, 127

threshold. Therefore it may happen that if a presynaptic neuron fires, and if the corresponding postsynaptic neurons have a potential close to the threshold, then all the postsynaptic neurons fire at the exact same time. This phenomenon can be massive (32, 33): this corresponds to the mathematical phenomenon of blow-up, which happens for some mean-field limits of such models. In this case, no time asynchrony is possible but such phenomenon is completely unrealistic from a biological point of view. There are LIF models with random or soft threshold (19, 23) which might not have this problem and which may also satisfy time asynchrony.

the neurons fire when their membrane potential reaches a fixed

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In (21), we proposed a discrete-event algorithm to simulate point processes with stochastic intensities. This algorithm is based on the theory of local independence graph (34), which is the directed neuronal network in our present case.

The algorithm works as follows (see Figure 1b). The spike 144 events happen in continuous time in the system (up to the 145 numerical precision). Once a spike on a particular presynaptic 146 neuron happens (red dots in Figure 1b), the postsynaptic 147 neurons are updated (orange dots in Figure 1b). The presy-148 naptic and the post synaptic neurons compute their intensities 149 (assimilated to membrane potential) and forecast its evolution 150 (green arrows in Figure 1b) if nothing in between occurs in 151 the system. They are therefore able to forecast their potential 152 next spike (gray dots in Figure 1b). The algorithm maintains 153 a scheduler containing all potential next spikes on all neurons 154 and decides that the next neuron to fire effectively is the one 155 corresponding to the minimum of these potential next spikes. 156 For more details, we refer to (21). 157

The gain comes from the fact that neurons that are not firing a lot, do not require a lot of computation either. In particular we do not have to update all neurons at each spike but only the pre and post synaptic neurons that are involved in the spiking event. This is the main difference with the parallel simulation framework detailed above. The other difference is that we can work with arbitrary precision, typically 10^{-15} if necessary, without impeding the time complexity of the algorithm.

Note that the whole algorithm is possible only because two neurons in the network will not spike at the same time: the whole concept is based on time asynchrony to be able to 169 jump from one spike in the system to the next spike in the 170 system. Of course, this is true only up to numerical precision: 171 if two potential next spikes (gray dots on Figure 1b) happen 172 at the exact same time with resolution 10^{-15} , by convention 173 the neuron with the smaller index is said to fire. But the 174 probability of such event is so small that this is not putting 175 the simulation in jeopardy.

Also note that this does not prevent neurons to eventually 177 synchronize frequently over a small time duration of a few 178 milliseconds, as defined for instance in (35) and the references 179 therein. 180

Procedural connectivity. One of the memory burden of both 181 methods (parallel and time asynchrony) comes from the fact 182 that a classic implementation stores the whole connectivity 183 graph, which is huge for brain scale models. 184

If the connectivity is the result of a random graph and 185 that each presynaptic neuron is randomly connected to its 186 postsynaptic neurons, one can store the random seed instead 187 of the result of the random attribution. Hence the whole 188

graph is never stored in full but only regenerated when need 189 be (see Figure 1b). The random connectivity is regenerated 190 at each spike taking advantage of the deterministic nature of 191 the pseudo-random generator used in the simulation. Storing 192 193 the generator initial seed, the seed of each neuron is computed 194 based on initial seed value and neuron index (see Figure 1c). With this method, only the initial seed is stored in memory. 195 Of course this dynamic regeneration at each spike has a cost 196 in terms of time complexity, but this cost is negligible with 197 respect to the other computations that need to be made and 198 this saves memory. 199

This method has been evoked at first in (23) for time asynchronous algorithms, without being put into practice, whereas this method has been already implemented with success on parallel programming with GPU (24).

Computational and memory costs. In (21), we obtained an accurate estimate of the complexity of the algorithm without procedural connectivity, for the simulation of linear Hawkes processes (*cf.* Equation 7 of (21)). This can be reused to compute the computational complexity of the same model, when the procedural connectivity step is added. Thus the overall time complexity of our algorithm is of the order of

$$\mathcal{O}\left(T\left[Md^2\bar{m}^2 + \log(M)Md\bar{m} + Md\bar{m}\right]\right)$$
[1]

where M is the number of neurons, p the connection probability, $d = \lceil pM \rceil$ the average degree of the network, \bar{m} the average firing rate of the network and T the simulation duration. The last term in Eq. (1) corresponds to the computational cost of the procedural connectivity at each spike, which is indeed negligible with respect to other terms, as explained before.

Note that such computational costs depend in particular
on the intensity shape of the underlying point process model.
The linearity of the Hawkes processes makes it easy to derive,
whereas this can be much more cumbersome with other models
such as stochastic LIF, which needs to compute the distribution
of the time at which the threshold is reached.

The maximal memory cost of the procedural connectivity, without the spike times storage, is of the order of $\mathcal{O}(d\omega) = \mathcal{O}(pM\omega)$, with ω the number of bits necessary for representing the index of a post-synaptic neuron.

The memory cost of a static storage of the whole graph is 228 of the order of $\mathcal{O}(dM\omega) = \mathcal{O}(pM^2\omega)$. We do not include in 229 this the memory costs for the storage of each spike of each 230 neuron. However, this cost is the same whatever the method 231 and it is of the order of $MT\bar{m}\epsilon$, where ϵ is the number of bits 232 necessary to represent a spike, which depends on the numerical 233 precision with which time is recorded. If d is thought to be a 234 fixed parameter, the memory cost of our complete algorithm 235 with procedural connectivity is thus 236

$$\mathcal{O}(d\omega + MT\bar{m}\epsilon)$$
 [2]

²³⁸ Conversely, the use of a static storage of the network is ²³⁹ $\mathcal{O}(dM\omega + MT\bar{m}\epsilon)$. Note however that depending on what ²⁴⁰ the program needs to return, we might not want to have the ²⁴¹ whole set of points but only summary statistics such as firing ²⁴² rates that will cost in memory much less than $\mathcal{O}(MT\bar{m}\epsilon)$.

243 Choice of brain scale parameters. Because of the precision of 244 the actual measurements and the brain region and neuron

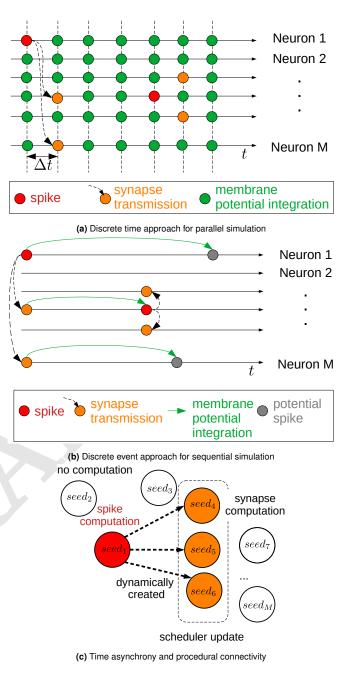


Fig. 1. Neuronal computations in time and in the network

variability, it is difficult to estimate quantitatively both physi-245 ological (number of synapses per neuron, etc.) and dynamic 246 parameters (average firing rate, etc.) of neuronal networks 247 in primates (6) and humans (36). Only rough estimates are 248 available. The human brain being the more computationally 249 intensive, we estimate here its main parameters for simulation. 250 Our goal is indeed to show the algorithm scalability to simulate 251 large networks with such parameters. 252

To our knowledge, the best documented region of the human brain is the (neo)cortex. Based on the structural statistics (number of neurons and synaptic connections) of neuronal networks in the (neo)cortex, we extrapolate here their representative parameter values at brain scale.

The *firing rate of a neuron* in the brain can be estimated 258

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by the limited resources at its disposal, especially glucose. Measures of ATP consumption have shown (see (29)) that the firing rate of a neuron in human neocortex can be estimated around 0.16Hz. Still based on ATP consumption, only 10% of the neurons in the neocortex can be active at the same time.

So it seems coherent to choose an average of 0.16Hz. These values can be extrapolated to the whole brain^{*}, as follows.

The neocortex represents 80% of the volume of the brain (37) and consumes 44% of its energy (29). Considering that the energy consumed by the brain is proportional to the firing rate of the neurons, the power ratio then consists of

$$rac{P_{cortex}}{P_{brain}} \sim rac{V_{cortex} ar{m}_{cortex}}{V_{brain} ar{m}_{brain}},$$

with \bar{m}_{cortex} the mean firing rate of individual neurons in the neocortex (resp. in the brain) and V_{cortex} the volume of the neocortex (resp. in the brain). The average firing rate of the brain then consists of $\bar{m}_{brain} = 0.8 \times \frac{0.16}{0.44} = 0.29$ Hz per neuron.

This average firing rate should not be confused with the 271 fact that particular neurons can have a much larger firing 272 rate. Particularly, groups of neurons synchronize together for 273 achieving a particular cognitive task: this is the concept of 274 neuronal assemblies (38). In an assembly, neurons can usually 275 increase their rates to tens Hz (possibly 50Hz) over a short 276 duration. Therefore, we choose a *firing rate in the brain* where 277 most of the neurons have a firing rate of 0.3Hz but some have 278 a much higher firing rate (up to 50Hz) using an heavy tailed 279 distribution, see Materials and Methods and Table 2. 280

The average number of synaptic connections in human 281 brains is hard to estimate and depends heavily on the neuron 282 types and brain regions. For example, in the brain, it is as-283 sumed that the majority of neurons are cerebellum granule 284 cells (39). In (40), the number of synaptic connections to gran-285 ule neurons is estimated to an average of only 4 connections, 286 matching those observed anatomically. On the other hand, 287 Purkinje neurons can have up to 200,000 synapses on only one 288 dendrite in the human brain (39). The approximate number 289 of synapses in the cortex is 0.6×10^{14} (41). Assuming that 290 the volume of the cortex represents around 80% of the volume 291 of the brain, the number of synapses in the brain is of order 292 10^{14} . Considering that the number of neurons in the human 293 brain is of order 10^{11} (36), we find that the average number of 294 synapses is about 1,000 synapses per neuron^{\dagger}. The synaptic 295 connection probability thus depends on the number of neurons 296 $M: p_M = \frac{1,000}{M}.$ 297

Finally, an action potential arriving on one pre-synaptic neuron produces an Excitatory PostSynaptic Potential (EPSP), or an Inhibitory PostSynaptic Potential (IPSP), in the postsynaptic neuron. The duration of these postsynaptic potentials is about $\tau = 20ms$ (39).

Therefore the parameters that we used in the simulation are indicated in Table 1. Notice that these parameters are generic and intuitive and can be taken easily into account in further studies, either at a biological or at theoretical model level. Table 1. Neuronal network parameters at human brain scale level.

Software and hardware configurations. The simulations have 308 been run on a Symmetric shared Memory multiProcessor 309 (SMP) computer equipped with Intel CascadeLake@2.6GHz 310 processors[‡]. This kind of computer is used here to have access 311 to larger memory capacities. At computational level, only 312 one processor was used for the simulations. For small sizes 313 of networks requiring small amounts of memory (cf. Figure 314 3b), e.g. a network of 10^6 neurons with a total of 10^9 synaptic 315 connections, this computer is equivalent to a simple desktop 316 computer. The simulation of such networks takes only 25 317 minutes for each biological second. This is of the order of 318 the 4.13×10^6 neurons and 24.2×10^9 synapses simulated on 319 GPUs (24), which takes about 15 minutes for each biological 320 second. This GPU-based simulation was already running up 321 to 35% faster than on 1024 supercomputer nodes (one rack of 322 an IBM Blue Gene/Q) (42). Our simulation only requires a 323 single usual processor and no GPU. 324

The implementation of the algorithm is written in C++ 322 (2011) programming language and compiled using g++ 9.3.0. 326

Firing rate at network level. Table 2 presents classical elemen-327 tary statistics on the simulated firing rates, whereas Figure 2 328 presents the corresponding densities. As one can see in Section 329 Material and Methods, the system is initialized with a lot of 330 neurons whose spontaneous spiking activity is null. The sys-331 tem needs to warm up to have almost all neurons spiking. This 332 explains why the density at T = 5s is still rippled whereas, at 333 T = 50s, it looks much smoother. This last case corresponds 334 basically to the stationary version of the process. Indeed, as 335 explained in Section Material and Methods, the parameters 336 of the Hawkes model (in particular the spontaneous spiking 337 activity) have been fixed to achieve a certain stationary distri-338 bution of the firing rates (with mean 0.3Hz), which is heavy 339 tailed to achieve records as large as 50 Hz. As one can see 340 (even if at T = 5s the system is not warmed up yet with a 341 lot of non spiking neurons), one can still achieve the desired 342 average firing rate and extremal values. These basic statistics 343 are not varying a lot with T (see Table 2). Note that the 344 density plots are roughly the same for all configurations: with 345 ripples at T = 5s and smooth curve at T = 50s. 346

Our approach is particularly adapted to simulate precisely and efficiently a huge disparity in frequency distributions. Indeed, our simulation algorithm (22) allows focusing efficiently the computing resources on highly spiking neurons without computing anything for almost silent neurons (*cf.* Figures 1a and 1b). The last advantage of our approach is to be able to store time stamps with a precision of $10^{-15}s$. 353

Execution times and memory usage. The simulation execution times are presented in Figure 3a for different sizes of

^{*}This calculus can be found on AI impact project webpage: https://aiimpacts.org. rate-of-neuron-firing/ (lastly verified: 02/09/2021)

[†] Calculus on Al impact project webpage: https://aiimpacts.org/scale-of-the-human-brain/ (lastly verified: 02/09/2021).

[‡]We used v100l and v100xl partitions on Joliot-Curie supercomputer at TGCC as a Fenix Infrastructure resource. Each node of v100l and v100xl has Intel CascadeLake@2.6GHz processors. A node on v100l is a dual-socket one with 2x18 cores, each core having a memory of 10 GBytes, so the total amount of available memory is 360 GBytes. A node on v100xl is a quad-socket one with 4x18 cores, each core having a memory of 41.5 GBytes, so the total amount of available memory is 3 TBytes.

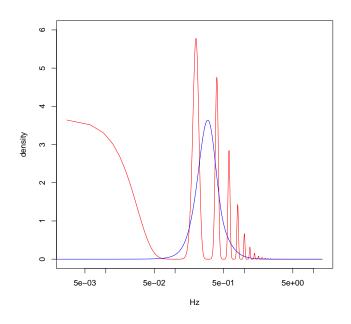


Fig. 2. Densities (on a logarithmic scale) of the simulated firing rates in the network with $M = 10^6$ neurons and d = 1000 post-synaptic connections in average. In red, for T = 5s and in blue for T = 50s. These densities are obtained with a Gaussian kernel estimator with bandwidth 0.02.

neural networks and different numbers of synaptic connec-356 tions (called children). The experimental execution times 357 obtained are in agreement with Eq. (1) which predicts, for 358 instance, $O(10^{12})$ operations for $M = 10^7$ and $d = 10^3$. The 359 curves are almost linear (with slopes around 1.1) with respect 360 to the number of neurons, for different numbers of synaptic 361 connections. 362

The total amount of memory used is displayed in Figure 3b. 363 They are in agreement with the procedural memory complexity 364 of Eq. (2) and also almost linear (with slopes slightly below 365 1). Note in particular that for $M = 10^7$, $d = 10^3$, $\omega = 32$ and 366 $\epsilon = 64$ (leading to a 10^{-15} precision in time), the memory cost 367 predicted by Eq. (2) is $O(10^{11})$ for the static implementation, 368 whereas it is $O(10^9)$ for the procedural connectivity imple-369 mentation. Besides notice that, as expected, increasing the 370

М	d	Average freq.	Freq. min.	Freq. max.	Freq. std.	Percentage of non spiking neuron
1e5	250	0.279 (0.279)	0 (0)	14 (13.94)	0.315 (0.222)	31.2 (0.01)
1e5	500	0.334 (0.333)	0 (0.02)	6.6 (5.76)	0.328 (0.218)	23.5 (0)
1e5	1000	0.399 (0.398)	0 (0.04)	10.4 (11.64)	0.345 (0.220)	16.9 (0)
1e6	250	0.267 (0.267)	0 (0)	19.2 (20.84)	0.308 (0.217)	33 (0.01)
1e6	500	0.322 (0.324)	0 (0)	38.4 (39.38)	0.329 (0.225)	25.1 (0.00)
1e6	1000	0.383 (0.387)	0 (0.02)	13.4 (12.9)	0.344 (0.223)	18.5 (0)
5e6	250	0.26 (0.261)	0 (0)	27.4 (28.5)	0.307 (0.217)	34.1 (0.02)
5e6	500	0.315 (0.316)	0 (0)	34.2 (34.1)	0.324 (0.220)	26 (0.00)
5e6	1000	0.377	0	19.8	0.342	19
1e7	250	0.258 (0.259)	0 (0)	23.2 (21.62)	0.306 (0.217)	34.4 (0.02)
1e7	500	0.311	0	21.6	0.322	26.4
1e7	1000	0.374	0	21.8	0.342	19.3
5e7	250	0.253	0	38.2	0.304	35.4
5e7	500	0.305	0	50.6	0.321	27.2
1e8	250	0.251	0	46.2	0.303	35.7

Table 2. Firing rates elementary statistics obtained by simulation for different sizes of neural networks and different numbers of synaptic connections and T = 5s. The number between parentheses displays the results at T = 50s for the less complex simulations

average number of post-synaptic connections per neuron has 371 few impact on the memory. Indeed, within the network, only 372 the post-synaptic connections receiving spikes are dynamically 373 generated. 374

Material and Methods

Model. For a set of M neurons, we first design the graph of 376 interaction by saying that neuron j influences neuron i if 377 a Bernoulli variable $Z_{j \to i}$ of parameter p is non zero. The 378 resulting network is an Erdös-Rényii graph. 379

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Once the network is fixed, we design the spike apparition thanks to a Hawkes process, that is a point process whose intensity is given by

$$\lambda^{i}(t) = \nu_{i} + \sum_{j=1}^{M} \int_{0}^{t} h_{j \to i}(t-\tau) dN_{\tau}^{j},$$

with dN^{j} the point measure associated to neuron j. In this 380 formula, ν_i represents the spontaneous firing rate of the neuron 381 *i* if the other neurons do not fire, whereas $h_{j\to i}$ is the interac-382 tion function, that is $h_{j\to i}(u)$ is the increase (if positive) or 383 decrease (if negative) that the firing rate of neuron i suffers 384 due to a spike on j, which happens u seconds before. 385

We are interested in a particular case of the Hawkes process where all the interaction functions are always the same when they are non null. More precisely, we set the interaction function

$$h_{j \to i} = Z_{j \to i} \theta h,$$

where h is a fixed positive interaction function of integral 1, θ is 386 a tuning parameter that we need to calibrate to avoid explosion 387 of the process. We also set $h_{i\to i} = 0$ (no self interaction). We 388 take $h = 501_{[0,0,02]}$: the interaction function is a constant 389 and non zero only on a small interval of length 20ms, which 390 391

corresponds to typical Post Synaptic Potentials in the brain. Let us denote $H_{j\to i} = \int_0^{+\infty} h_{j\to i}(t)dt$ and $H = (H_{j\to i})_{i,j=1,\dots,M}$ is the corresponding matrix (line *i* corre-392 393 sponds to a triggered neuron, column j to a triggering neuron). 394

Note in particular that in this model, there are only excita-395 tory neurons : if in the brain, there are inhibitory neurons, this 396 will only reduce the number of points without changing the 397 complexity. Moreover when all the interaction functions are 398 non negative, we can easily understand the explosion condition. 399

Indeed, this Hawkes process explodes, that is, it produces 400 an exponentially increasing number of point per unit of time 401 (see (43)) if the spectral radius of H is larger than 1. 402

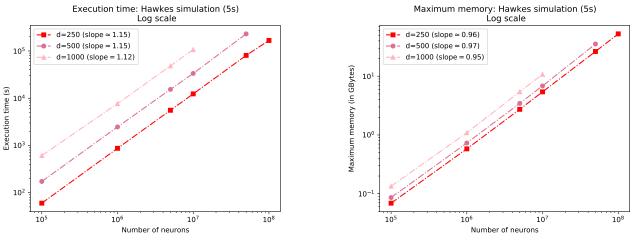
If (*Condition Stat*) the spectral radius is strictly smaller 403 than 1 (44), then a stationary version exists and the corre-404 sponding vector of mean firing rates $m = (m_i)_{i=1,...,M}$ is given 405 bv

$$m = (I - H)^{-1} \nu.$$
 [3] 407

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Note also that if we start the simulation without points before 408 0 in (*Condition Stat*), the process is not stricto sensu stationary 409 but it will converge to an equilibrium given by the stationary 410 state (ergodic theorem) and that the number of points that 411 will be produced is always smaller than the stationary version. 412

In the present case we want (i) to prevent explosion and 413 (ii) to reach a certain vector m which is biologically realistic 414 (average around 0.3 Hz, records around 50 Hz). Both of these 415 calibrations can be done mathematically beforehand in the 416 Hawkes model : we can guarantee the behavior of the whole 417



(a) Simulation execution times for different sizes of networks.

(b) Memory usages for different sizes of networks.

Fig. 3. Simulation execution times (3a) and memory usage (3b) for different sizes of networks.

418 system even before performing the simulation, whereas this419 might be much more intricate for other models such as LIF.

420 **Choice of** θ **or how to avoid explosion.** Note that $H = \theta \mathcal{Z}$, 421 with $\mathcal{Z} = (Z_{j \to i})_{i,j=1,...,M}$. So if we can compute the largest 422 eigenvalue of \mathcal{Z} or an upper bound, we can decide how to 423 choose θ .

We can use Gershgorin circles (45) to say that any complex eigenvalue λ of \mathcal{Z} satisfies (because the diagonal is null),

$$|\lambda| \le \max_{i=1,\dots,M} \sum_{j \ne i} Z_{j \to i}.$$

Therefore the spectral radius is upper bounded by 424 $\max_{i=1,...,M} B_i$, where $B_i = \sum_{j \neq i} Z_{j \to i}$. This random quantity can be computed for small networks but it is clearly too 425 426 intensive in our setting: indeed, with the procedural connec-427 tivity implementation, it is always easy to access the children 428 ℓ of a given *i*, i.e. such that $i \to \ell$ is in the graph, but we need 429 to look at all the neurons in the graphs to find out the set of 430 parents *j* of *i*, i.e. such that $j \rightarrow i$ is in the graph. However, 431 probabilistic estimates might be computed mathematically. 432 Indeed B_i is just a sum of i.i.d. Bernoulli variables. So we 433 can apply Bernstein's inequality (46). This leads to, for all 434 positive x, 435

36
$$\forall i = 1, ..., M,$$

37 $\mathbb{P}(B_i \ge (M-1)p + \sqrt{2(M-1)p(1-p)x} + x/3) \le e^{-x},$

and, by union bound, for the maximum

$$\mathbb{P}(\max_{i=1,\dots,M} B_i \ge (M-1)p + \sqrt{2(M-1)p(1-p)x} + x/3) \le Me^{-x}.$$

Therefore let us fix a level α , say 1%, and take $x = \log(M) + \log(1/\alpha)$ in the previous equation. We obtain that with probability larger than $1 - \alpha$, the spectral radius of \mathcal{Z} is upper bounded

$$\rho_{\max} = (M-1)p + \xi_{\alpha}$$

with

$$\xi_{\alpha} = \sqrt{2(M-1)p(1-p)[\log(M) + \log(1/\alpha)]} + [\log(M) + \log(1/\alpha)]/3$$

Note that ρ_{max} is roughly (M-1)p, which is the largest eigenvalue of $\mathbb{E}(\mathcal{Z})$. Finally it means that if we take $\theta < \frac{438}{1}$ $1/\rho_{\text{max}}$, the process will not explode with probability larger than $1-\alpha$. In practice, to ensure a strong enough interaction, we take $\theta = 0.9\rho_{max}^{-1}$.

Choice of ν_i or how to constraint the distribution of the mean 443 firing rates. The first step consists in deciding for a target 444 distribution for the m_i . We have chosen to pick the m_i 's 445 independently as 0.1X where X is the absolute value of a 446 student variable with mean 3 and 4 degrees of freedom. The 447 choice of the student variable was driven by the wish of having 448 a moderate heavy tail, which will ensure records around 50 449 Hz and a mean around 0.3Hz. 450

The problem is that the m_i 's are not parameters of the model, so we need to understand how to tune ν_i to get such m_i 's. Note that by inverting Eq. (3), we get that

$$(I - H)m = \nu$$

that is for all \boldsymbol{i}

$$\nu_i = m_i - \theta \sum_{j \neq i} m_j Z_{j \to i},$$

which is very intuitive (47). Indeed the spontaneous rate that we need to put is the mean firing rate m_i minus what can be explained with the parents of *i*.

So in theory, the Hawkes model is very easy to tune for prescribed firing rates since there is a linear relationship between both. However, and for the same reasons as before, it might be too computationally intensive to compute this explicitly.

One possible way is to again use concentration inequalities, but this time on $\sum_{j \neq i} m_j Z_{j \rightarrow i}$ and not on B_i . However we decided to do something simpler, which works well (as seen in Figure 2). ⁴⁶² Indeed $\sum_{j \neq i} m_j Z_{j \to i}$ is a sum of about $(M-1)p \simeq 1000$ ⁴⁶³ i.i.d variables with mean $\bar{m} = 0.3$ Hz. Hence it should be close ⁴⁶⁴ to $\bar{m}B_i$. With the previous computations, we know already ⁴⁶⁵ that ν_i should therefore be larger than $m_i - \theta \rho_{\max} \bar{m}$.

With the previous choice of $\theta = 0.9\rho_{\text{max}}^{-1}$, we have chosen to take the positive part for the ν_i 's in the simulation, that is :

$$\nu_i = \max(m_i - 0.9\bar{m}, 0).$$

Therefore ν_i remains positive or null, which guarantees that 466 the Hawkes process stays linear. However, this also means 467 that a non negligible portion of the neurons start with a null 468 spontaneous firing rate, which explains the ripples of Figure 2. 469 With this choice, we cannot hope to have exactly the same 470 distribution as the desired m_i 's, but it conserves the same 471 heavy tail and roughly the same mean firing rate as the one 472 we wanted, as one can see on Table 2. 473

474 Discussion

Thanks to time asynchrony, we propose a new scalable algo-475 rithm to the simulate spiking activity of neuronal networks. 476 We are able to generate roughly the same firing pattern as a 477 real brain for a range between 10^5 and 10^8 neurons, in a few 478 minutes on a single processor, most parameters being tuned 479 thanks to general considerations inferred from the literature. 480 Corresponding computational and memory complexities are 481 shown to be both linear. 482

At simulation level, whereas usual simulations are based 483 on the continuous variation of the electrical potentials of LIF 484 neurons, point processes lead to much more efficient simula-485 tions. In particular, instead of computing the small continuous 486 variations for all neurons, only discrete spikes and their in-487 teractions are simulated in the network. Between two spikes 488 no computations are done. Point processes also lead to time 489 asynchrony (two spikes cannot occur at the same time in the 490 network), which is a fundamental hypothesis for the algorithm 491 to work. 492

Combining the time asynchrony hypothesis with procedural 493 connectivity drastically reduces the memory consumption and 494 also, for the same network activity, reduces the computations 495 per spikes (cf. Figures 1a and 1b). In particular, complexities 496 (both theoretical and concrete) can be computed and proved 497 to be almost linear in the number of neurons, when Hawkes 498 processes are generated, leading to simulation scalability of 499 the whole approach without precision loss. 500

Both modeling and simulation results open many research perspectives. We are currently developing new discrete event algorithms that are able to simulate the spiking activity of neurons embedded in potentially infinite neuronal networks (48). This paves the path for simulation of parts of the brain as an open physical system.

Furthermore, the minimal number of computations and
memory storage obtained here open new exciting perspectives
with respect to massive neuromorphic computers, by improving
the energy saving consumption of neuromorphic components
(49).

Finally, if we have proved that the simulation is doable, the point process model used here can be calibrated further on real data, by incorporating inhibition and more variability in the interaction functions. Also, this model can be used for reconstructing the functional connectivity of experimentally recorded neurons (15, 47) to have access to more realistic interaction functions. Besides, as only few computing resources (one single processor) is used with a minimal memory amount, this opens new possibilities to run in parallel many independent replications of stochastic simulations of large networks. This is particularly interesting for calibrating models based on real data collections.

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 K Amunts, et al., The human brain project—synergy between neuroscience, computing, informatics, and brain-inspired technologies. <u>PLoS biology</u> 17, e3000344 (2019). 536

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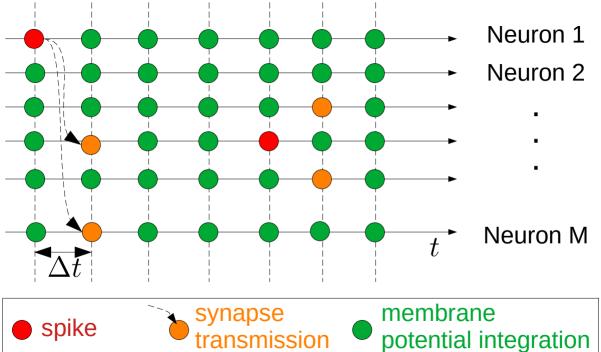
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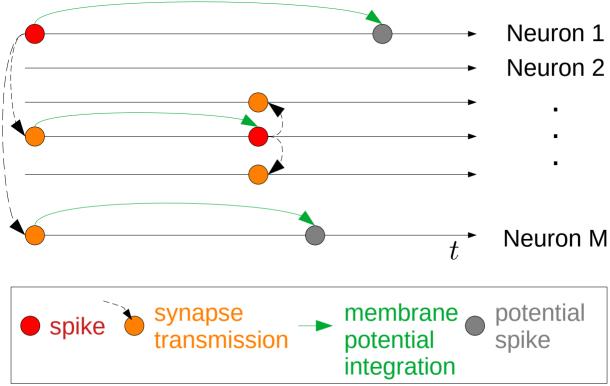
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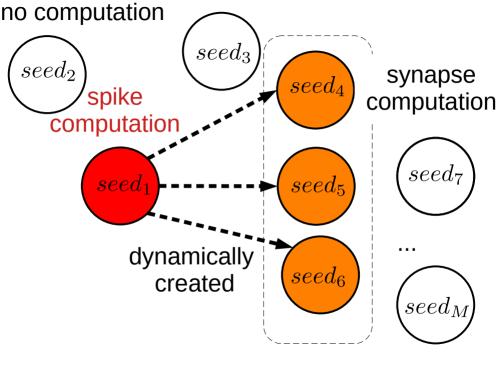
- 2. MR Dando, Japan's brain/minds project (2020).
- W Koroshetz, et al., The state of the nih brain initiative. <u>J. Neurosci.</u> 38, 6427–6438 (2018).
 RR Netz, WA Eaton, Estimating computational limits on theoretical descriptions of biological cells. PNAS 118 (2021).
- E Gal, et al., Rich cell-type-specific network topology in neocortical microcircuitry. Nat. Neurosci. 20, 1004–1013 (2017).
- S Herculano-Houzel, CE Collins, P Wong, JH Kaas, Cellular scaling rules for primate brains. <u>Proc. Natl. Acad. Sci.</u> 104, 3562–3567 (2007).
- DA McCormick, Y Shu, Y Yu, Hodgkin and huxley model—still standing? <u>Nature</u> 445, E1–E2 (2007).
- J Guckenheimer, RA Oliva, Chaos in the hodgkin–huxley model. <u>SIAM J. on Appl. Dyn. Syst.</u> 1, 105–114 (2002).
- L Lapicque, Recherches quantitatives sur l'excitation electrique des nerfs traitee comme une polarization. <u>J. Physiol. Pathololgy</u> 9, 620–635 (1907).
- 10. H Yamaura, J Igarashi, T Yamazaki, Simulation of a human-scale cerebellar network model on the k computer. Front. neuroinformatics 14, 16 (2020).
- 11. RF Fox, Stochastic versions of the hodgkin-huxley equations. <u>Biophys. journal</u> 72, 2068–2074 (1997).
- AA Lazar, EA Pnevmatikakis, Reconstruction of sensory stimuli encoded with integrateand-fire neurons with random thresholds. <u>EURASIP J. on Adv. Signal Process</u>. 2009, 1–14 (2009).
- W Truccolo, UT Eden, MR Fellows, JP Donoghue, EN Brown, A point process framework for relating neural spiking activity to spiking history, neural ensemble, and extrinsic covariate effects. <u>J. Neurophysiol</u>. **93**, 1074–1089 (2005).
- EN Brown, R Barbieri, V Ventura, RE Kass, L Frank, The time-rescaling theorem and its application to neural spike train data analysis. <u>Neural Comput.</u> 14, 325–346 (2002).
- P Reynaud-Bouret, V Rivoirard, F Grammont, C Tuleau-Malot, Goodness-of-fit tests and nonparametric adaptive estimation for spike train analysis. <u>The J. Math. Neurosci.</u> 4, 3 (2014).
 J Pillow, et al., Spatio-temporal correlations and visual signalling in a complete neuronal
- P mow, et al., Spato-temporal constantions and visual signalling in a complete neuronal population. <u>Nature</u> **454**, 995–999 (2008).
 C Pouzat, A Chaffiol, Automatic spike train analysis and report generation. an implementation
- K. Galves, E. Löcherbach, Infinite systems of interacting chains with memory of variable
- A Gaives, E Lochetoach, Immile systems of interacting chains with heritory of variable length—a stochastic model for biological neural nets. J. Stat. Phys. 151, 896–921 (2013).
 L Sacerdote, MT Giraudo, Stochastic Biomathematical Models. (Lecture Notes in Mathemat-
- ics, Springer) Vol. 2058, pp. 99–148 (2013). 20. P Brémaud, Point processes and queues. (Springer-Verlag, New York-Berlin). (1981) Martin-
- P Brémaud, <u>Point processes and queues</u>. (Springer-Verlag, New York-Berlin), (1981) Martingale dynamics, Springer Series in Statistics.
- C Mascart, A Muzy, P Reynaud-bouret, Efficient simulation of sparse graphs of point processes (2020).
- A Muzy, Exploiting activity for the modeling and simulation of dynamics and learning processes in hierarchical (neurocognitive) systems. <u>Comput. Sci. Eng.</u> 21, 84–93 (2019).
- Grazieschi, Paolo, et al., Network of interacting neurons with random synaptic weights. <u>ESAIM: ProcS</u> 65, 445–475 (2019).
- 24. JC Knight, T Nowotny, Larger gpu-accelerated brain simulations with procedural connectivity. <u>Nat. Comput. Sci.</u> 1, 136—142 (2021).
- A Muzy, BP Zeigler, F Grammont, Iterative specification as a modeling and simulation formalism for i/o general systems. <u>IEEE Syst. J.</u> 12, 2982–2993 (2017).
- R Brette, et al., Simulation of networks of spiking neurons: a review of tools and strategies. J. computational neuroscience 23, 349–398 (2007).
- M Rudolph, A Destexhe, Analytical integrate-and-fire neuron models with conductance-based dynamics for event-driven simulation strategies. <u>Neural computation</u> 18, 2146–2210 (2006).
- JD Touboul, OD Faugeras, A markovian event-based framework for stochastic spiking neural networks. J. computational neuroscience 31, 485–507 (2011).
 P Lennie. The cost of cortical computation. Curr. Biol. 13, 493 – 497 (2003).
- P Lennie, The cost of cortical computation. <u>Curr. Biol.</u> 13, 493 497 (2003).
 A Duarte, A Galves, E Löcherbach, G Ost, Estimating the interaction graph of stochastic
- neural dynamics. <u>Bernoulli</u> 25, 771–792 (2019).
 P Jahn, RW Berg, Jr Hounsgaard, S Ditlevsen, Motoneuron membrane potentials follow a time inhomogeneous jump diffusion process. J. Comput. Neurosci. 31, 563–579 (2011).

- 597 32. MJ Cáceres, JA Carrillo, B Perthame, Analysis of nonlinear noisy integrate & fire neuron
- 598 models: blow-up and steady states. J. Math. Neurosci. 1, Art. 7, 33 (2011).
- F Delarue, J Inglis, S Rubenthaler, E Tanré, Global solvability of a networked integrate-andfire model of McKean-Vlasov type. <u>Ann. Appl. Probab.</u> 25, 2096–2133 (2015).
- 34. V Didelez, Graphical models of markes point processes based on local independence.
 J.R. Stat. Soc. B 70, 245–264 (2008).
- 35. C Tuleau-Malot, A Rouis, F Grammont, P Reynaud-Bouret, Multiple Tests Based on a
 Gaussian Approximation of the Unitary Events Method with Delayed Coincidence Count.
 <u>Neural Comput.</u> 26, 1408–1454 (2014).
- S Herculano-Houzel, R Lent, Isotropic fractionator: A simple, rapid method for the quantification of total cell and neuron numbers in the brain. J. Neurosci. 25, 2518–2521 (2005).
- 408 37. H Stephan, H Frahm, G Baron, New and revised data on volumes of brain structures in insectivores and primates. <u>Folia primatologica</u> 35, 1–29 (1981).
- 38. F Grammont, A Riehle, Spike synchronization and firing rate in a population of motor cortical neurons in relation to movement direction and reaction time. <u>Biol. cybernetics</u> 88, 360–373
 (2003).
- 613 39. GM Shepherd, <u>The synaptic organization of the brain</u>. (Oxford university press), (2004).
- A Litwin-Kumar, KD Harris, R Axel, H Sompolinsky, L Abbott, Optimal degrees of synaptic connectivity. <u>Neuron</u> 93, 1153–1164.e7 (2017).
- 41. DA Drachman, Do we have brain to spare? <u>Neurology</u> **64**, 2004–2005 (2005).
- 42. MO Gewaltig, M Diesmann, Nest (neural simulation tool). <u>Scholarpedia</u> **2**, 1430 (2007).
- 618
 43. S Delattre, N Fournier, M Hoffmann, Hawkes processes on large networks. Ann. App. Probab.

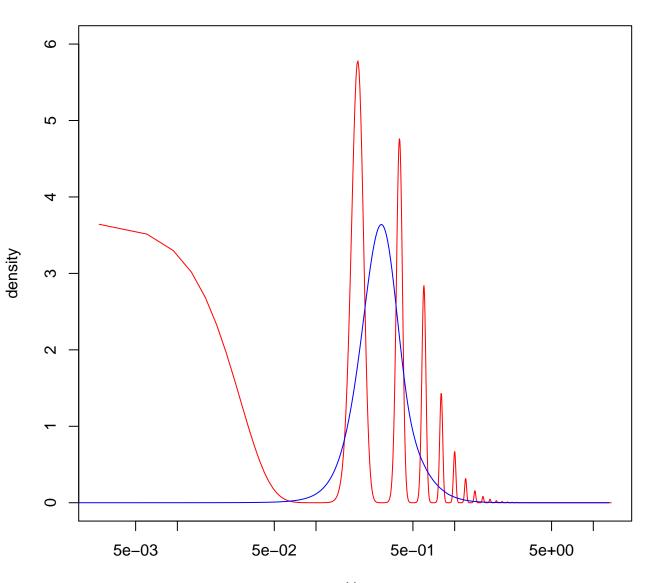
 619
 26, 216 261 (2016).
- 44. AG Hawkes, D Oakes, A cluster process representation of a self-exciting process.
 J. Appl. Probab. 11, 493–503 (1974).
- R Varga, <u>Gershgorin and his circles</u>. (Springer-Verlag), (2004) Springer Series in Computational Mathematics.
- 46. S Boucheron, G Lugosi, P Massart, <u>Concentration inequalities</u>. (Oxford University Press,
- Oxford), (2013) A nonasymptotic theory of independence, With a foreword by Michel Ledoux.
 P Reynaud-Bouret, A Muzy, I Bethus, Towards a mathematical definition of functional connectivity. (2021).
- TC Phi, A Muzy, P Reynaud-Bouret, Event-Scheduling Algorithms with Kalikow Decomposition for Simulating Potentially Infinite Neuronal Networks. <u>SN Computer Science</u> 1 (2020).
- 49. LA Plana, et al., spinnlink: Fpga-based interconnect for the million-core spinnaker system.
 <u>IEEE Access 8</u>, 84918–84928 (2020).







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