Packetization improves communication efficiency in brain networks with rapid and cost-effective propagation strategies

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Abstract

Methodological developments in neuroscience and neuroimaging have allowed mapping large-scale networks of white matter structural connections across the whole brain. Many computational studies have built dynamic models of cortical communication processes in these networks to gain insights into generative mechanisms of complex brain functions. When modeling the communication dynamics in brain networks, various approximations have been applied to the manner of cortical signal propagation. For example, existing communication models assume that cortical signals propagate over the network by following, e.g., random walk and shortest path strategies. Recent studies argue that propagation strategies that enable rapid communication but only need a small information cost for reaching the destination are physiologically plausible. Another approximation lies in the assumption of whether cortical signals are packetized or not during propagation (in analogy to packet switching or message switching, respectively, in the context of telecommunications). Most previous models rely on the approximation that message switching is used; however, the plausibility of both switching architectures has not been as extensively studied as that of propagation strategies. To address this issue, we evaluate the plausibility of switching architectures by examining in simulations which of them achieves faster (more efficient) communication in brain networks with the plausible propagation strategies. We performed discrete-event simulations on a macaque brain network and compared the communication efficiency between message switching and packet switching for several propagation strategies. We find that packet switching leads to better communication efficiency when the signals propagate over brain networks under rapid and cost-effective strategies, such as informed and biased versions of random walks. This result suggests that packet switching is more plausible for building brain network communication models. Our study provides novel insights into how to approximate the communication dynamics in large-scale brain networks.

Introduction

Advancements in a broad range of methodologies have allowed the mapping of white matter structural brain networks (the connectome) in the mammalian neocortex [1–5]. Previous studies have modeled the large-scale dynamics in brain networks to understand the neural origins of complex brain functions [6]. Models of such dynamics can be broadly categorized into two groups. The first group consists of biophysical models in which regional models of neuronal population dynamics (e.g., oscillator models or neural mass models) are coupled based on interregional connectivity patterns in brain networks [7–12]. Ongoing large-scale brain dynamics are simulated by numerically solving differential equations in these models, and many empirical properties of functional imaging data (especially those related to resting-state functional brain connectivity [13–15]) have been replicated in simulations [16]. The second group, on which we focus in this study, is composed of non-biophysical models that describe the communication dynamics of cortical regions by the flow of abstract discrete signals over brain networks [17–25]. These models rely on rather simple approximations of the communication dynamics in brain networks, whereas they permit modeling signal propagation in networks more directly compared to the first group of models. Region-to-region communication metrics derived from the second group of models have also been shown to explain empirical data properties, such as the weights of resting-state functional brain connectivity [19, 22].

The communication dynamics in brain networks have been approximated with various signal propagation strategies. The physiological plausibility of propagation strategies can be discussed from the perspectives of communication speed and information cost [23–25]. In general, the speed of interregional communication in the cortex needs to be high enough to realize complex brain functions. At the same time, the amount of information required for cortical signals to propagate toward the destination region (referred to as the information cost) should be limited to the extent that no knowledge of the global network topology is used [23]. Several network metrics in connectomics [26, 27] assume models in which communication takes place through the shortest paths between nodes (cortical regions), but that requires centralized knowledge of the global network topology. Alternative models are built on the basis that nervous systems are decentralized [17–22, 24]. A representative propagation strategy used in such models is the random walk [20, 21], where a signal is assumed to randomly propagate from a node to its neighboring nodes (structurally connected regions). The random walk (RW) and shortest path (SP) strategies are the limiting extremes in terms of communication speed and information cost [25]. In RW, no knowledge is required for signal propagation, but the communication between nodes can be slow, particularly for those located in two different modules (densely connected groups of nodes) [28]. In SP, the communication is typically fast, but full knowledge of the network topology is necessary for searching the shortest paths. Physiologically plausible propagation strategies may exist within these two extremes, enabling rapid and cost-effective communication in brain networks.

When approximating the communication dynamics in brain networks, one also needs to determine

whether cortical signals are packetized or not during their propagation [29, 30]. In most existing communication models, an entire signal, or a "message," is assumed to propagate simply without packetization, which is a form of signal transfer known as message switching in telecommunications [31]. On the other hand, Graham and Rockmore [29] proposed an Internet metaphor in which communication of cortical regions in brain networks takes place in a form corresponding to packet switching [31], the switching architecture widely used in the Internet. In packet switching, an entire message is split into smaller pieces, or "packets," allowing all packets in a message to individually take their own routes to the destination node where they are reassembled. Packet switching has several potential advantages, including its ability to reroute network traffic around busy or damaged nodes and its efficiency in systems relying on temporally sparse bursts of communication [29, 31]. Moreover, there is growing evidence in neurophysiology for packet-based communication in the cortex [32], and even a previous simulation study employing a message-based communication model [20] mentioned packet switching as a physiologically plausible alternative. Nonetheless, the plausibility of both switching architectures as a building block of brain network communication models has not been empirically evaluated, even in simulations.

Here, we assess the plausibility of message switching and packet switching in brain network communication models by examining which switching architecture allows for faster, i.e., more efficient, communication in brain networks with rapid and cost-effective propagation strategies. We stand on a hypothesis that a physiologically plausible switching architecture speeds up network communication with the plausible propagation strategies. Based on this hypothesis, we investigate whether packetization improves or degrades the communication efficiency in brain networks for various propagation strategies. We measure the communication efficiency from discrete-event simulations [33] of the signal flow through a large-scale cortical network in the macaque brain [34]. We start with the previous discrete-event simulation model in Mišić et al.[20, 21] for simulations of message switching and extend this model to simulate packet switching. As the strategies for signal propagation, we focus on RW (no knowledge required, but slow), SP (fast, but centralized knowledge required), and two RW-based strategies that exhibit intermediate properties between RW and SP in terms of communication speed and information cost. The first intermediate strategy is a set of informed versions of RW, which utilizes only local and decentralized information about the status of neighboring nodes (i.e., nodes directly connected to the node where the message or packet of interest is located). The second intermediate strategy is a biased version of RW [25], in which a parameter controls the transition probabilities of a message or packet to neighboring nodes from those of RW toward SP. In this study, we demonstrate that packetization improves the communication efficiency in brain networks with the informed and biased versions of RW.

Results

Simulating communication dynamics in brain networks

We simulated large-scale communication dynamics in a cortical white matter structural network derived from the Collation of Connectivity data on the Macaque brain (CoCoMac) database [1, 34–36] (Fig 1A). This brain network is the same as used in Mišić et al. [20, 21], who simulated the ongoing flow of abstract discrete signals over the network. These studies described cortical communication processes using a discrete-event simulation model with a queueing system [33] (Fig 1B). We followed their approach in our simulations of the communication dynamics with message switching and the RW strategy, where signals (messages) of equal length were randomly generated in time at gray matter source nodes in the brain network. To each message, a pair of source and destination nodes were randomly assigned. When RW was used as the propagation strategy, the message was randomly transmitted to one of the neighboring nodes until it arrived at its destination node. When other propagation strategies were used, the message was transmitted to a neighboring node under a given propagation strategy toward its destination node. Following the previous studies [20, 21], nodes in the network were modeled as servers with finite buffer capacity (maximum number of slots $H = 20$; see **Supplementary results** for the results without buffer size limitation). Once a message arrived at a node, it started service if there was no other message occupying that node, or it was stored in the buffer otherwise, forming a queue (see Fig 1B, bottom). When a previously occupying message finished its service, the newest message was to start its service (last-in-first-out, LIFO) [20, 21]. A message was removed from the network when it reached its destination node or when it was the oldest message in a fully occupied buffer and was ejected by a newly arriving message. We used the same arrival rate λ (average number of messages generated per time unit) and service rate μ (inverse of average service time) as in the previous studies [20, 21] ($\lambda = 0.01$ and $\mu = 0.02$). The setting of $\lambda < \mu$ prevented messages from overflowing in the network.

In the communication model of Mišić et al.[20, 21], an entire signal (message) was transmitted to a neighboring node at once by message switching [30]. We extended this model to simulate the communication dynamics through packet switching (Fig 1C). In our extended model, a message was divided into n equally sized packets. We ran simulations with $n = 5$ as the default for all packets and then $n = 3$ and $n = 10$ to check the reproducibility of the results (see **Supplementary results**). Packets of the same message were generated at once at the source node, and each packet was independently transmitted to a neighboring node under a given propagation strategy. All packets of the same message had the same destination but could take different routes to reach it. To take the size differences of messages and packets into account, we scaled the service rate μ and the maximum number of slots in the buffer H by n (see Fig 1C). Further details of the simulations are described in **Materials and methods**.

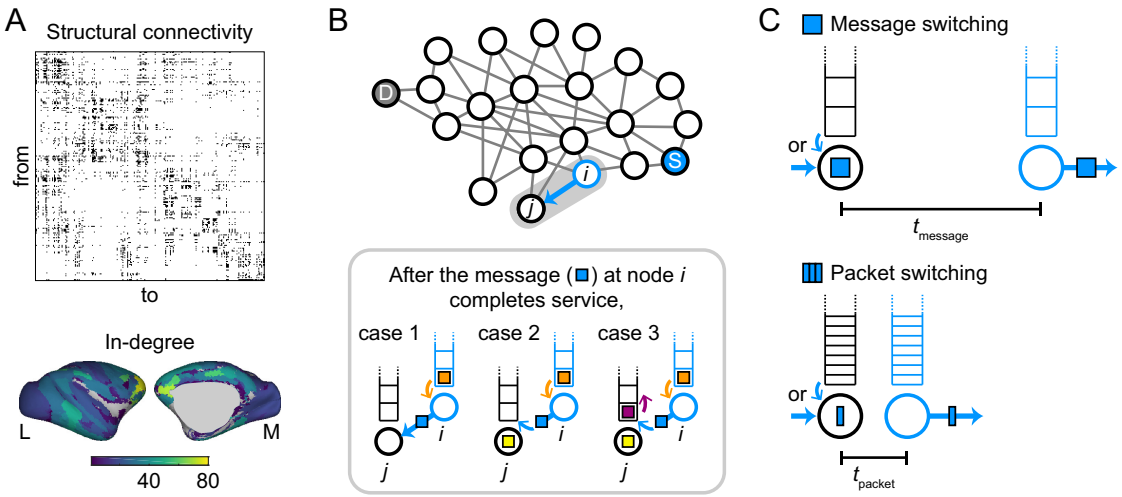

Fig 1 Discrete-event simulation of communication dynamics in a macaque brain network. (A) Adjacency matrix of the macaque brain network (242 cortical nodes, 4,090 binary and directed structural connections) [34] used in simulations (top) and rendering of its in-degree (the number of incoming connections to a node) on cortical surfaces (bottom left, lateral view; bottom right, medial view). The surface maps only show the in-degrees of the 187 nodes for which spatial coordinates are available [34]. (B) Schematic description of the discrete-event simulation. In simulations of signal propagation over the network, every signal (message) was associated with a randomly generated pair of source node S and destination node D. Once the message (colored light blue) completes service at node i, it is transmitted to node j and the message (orange) in the buffer of node i starts service at node i. If there is no signal at node j (case 1), the light-blue message starts service at node j. If another message (yellow) is in service at node j (cases 2 and 3), the arriving light-blue message is stored in the front of the buffer of node j. If a message (purple) is in the front of the buffer of node j (case 3), the purple message is moved to the back. (C) Extension from message switching to packet switching in the communication model. When a message is split into n equally sized packets, the service rate and the maximum number of slots in a buffer for a packet are specified as n times as large as those for a message. In this case, the service time for a packet (t_{packet}) is on average that for a message (t_{message}) divided by n.

Comparing communication efficiency between message switching and packet switching

Using the above simulation models with a given propagation strategy, we compared the communication efficiency in the brain network between message switching and packet switching. We evaluated the communication efficiency by measuring the elapsed time to transmit 100 messages or their corresponding sets of packets between source and destination nodes, i.e., the duration from when the first message or packet was generated in the network until the transmission of 100 messages or sets of packets to their destinations was completed. We considered the switching architecture having a shorter elapsed time as being more efficient.

As propagation strategies, we used RW, SP, and modified versions of RW that exhibit intermediate properties in terms of communication speed and information cost. As modified RW, we first investigated

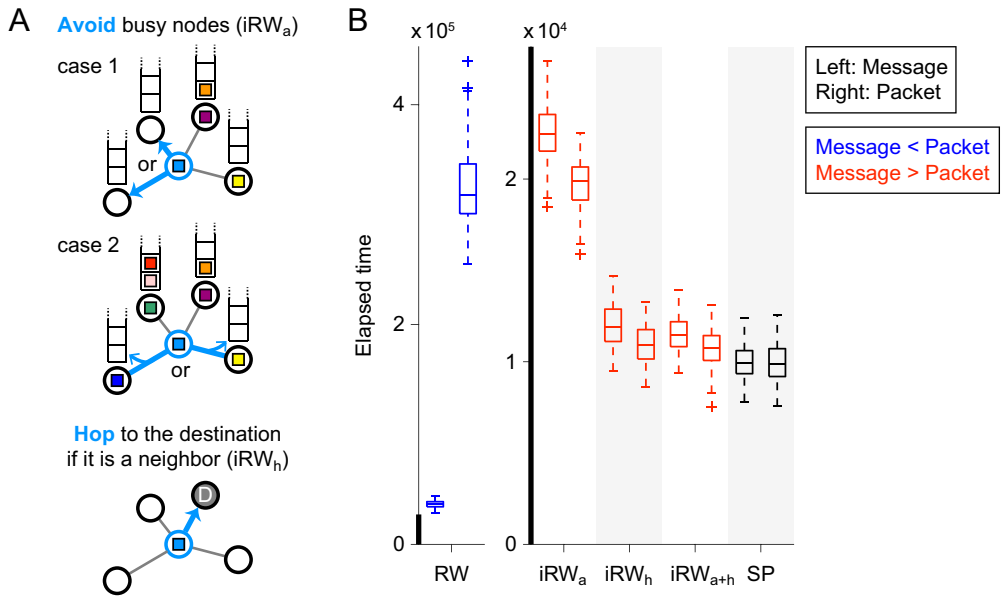

Fig 2 Simulations with the random walk (RW), informed random walk (iRW), and shortest path (SP) strategies. (A) Schematic description of iRW. In iRW with the rule of avoiding busy nodes (iRW_a and iRW_{a+h}), a message or packet is transmitted to a neighboring unoccupied node if it exists (case 1) or to the neighboring node with the minimum queue length in the buffer (case 2). In iRW with the rule of hopping to the neighboring destination node (iRW_h and iRW_{a+h}), a message or packet is directly transmitted to the destination node if it is included in the set of neighboring nodes. (B) Elapsed time for transmitting 100 messages or sets of packets under RW, iRW_a, iRW_h, iRW_{a+h}, and SP. The left and right boxplots for each propagation strategy show the elapsed times of message switching and packet switching, respectively (we ran 100 simulations to obtain the distribution of the elapsed time in each column). Boxplots are shown in red (blue) when the elapsed time of packet switching was shorter (longer) than that of message switching or in black when no significant differences were observed between them ($p < 0.05$, FDR corrected). The thick black lines in the vertical axes indicate the same range.

three informed versions of RW (iRW) that require information only from neighboring nodes for signal transfer (Fig 2A). The first version of iRW (iRW_a) was with a rule of avoiding busy neighboring nodes in transit. In this version, a message or packet was randomly transmitted to a neighboring node with no message or packet or, if such a node did not exist, to a neighboring node with the minimum queue length in the buffer. The second version of iRW (iRW_h) was with a rule of directly hopping to the destination node if it was one of the neighboring nodes. The combination of the above two rules were used in the third version of iRW (iRW_{a+h}).

Fig 2B shows the elapsed time for transmitting 100 messages or sets of packets with the propagation strategies RW, iRW_a, iRW_h, iRW_{a+h}, and SP. The elapsed time of packet switching was longer than that of message switching under RW (Mann-Whitney U test; $p = 1.28 \times 10^{-33}$, two-sided, false discovery rate (FDR) corrected by the Benjamini-Hochberg method; Cliff's delta $= 1$) and the elapsed times of both switching

architectures were similar under SP ($p = 0.848$, FDR corrected, Cliff's delta $= -0.016$). By contrast, the elapsed time of packet switching was shorter under iRW ($\mathrm{iRW_a}$, $p = 1.06 \times 10^{-24}$, FDR corrected, Cliff's delta $= -0.847$; $\mathrm{iRW_h}$, $p = 3.49 \times 10^{-7}$, FDR corrected, Cliff's delta $= -0.425$; $\mathrm{iRW_{a+h}}$, $p = 9.80 \times 10^{-7}$, FDR corrected, Cliff's delta $= -0.404$), indicating that packetizing messages improved the communication efficiency with iRW. Each version of iRW only needs information from neighboring nodes, but their elapsed times (especially those with $\mathrm{iRW_h}$ and $\mathrm{iRW_{a+h}}$) were much closer to the elapsed time with SP than that with RW. These results suggest that packetization makes communication in brain networks more efficient under rapid and cost-effective propagation strategies.

To confirm this finding, we replaced iRW with a biased version of RW (bRW) [25]. The bRW strategy has a control parameter c that can shift the propagation behavior from RW to SP. Fig 3A illustrates the transition probabilities under bRW in a toy example case. When a message or packet is transmitted to one of the neighboring nodes whose shortest path lengths to the destination node are (i) one, (ii) two, and (iii) three (Fig 3A, top), respectively, the transition probability to (i) is near $1/3$ (one over the number of neighboring nodes; RW-like behavior) when $c = 0.01$ and near 1 (SP-like behavior) when $c = 10$ (Fig 3A, bottom). For the formal definition of the transition probability under bRW, see **Materials and methods**. The shift of propagation behavior over the spectrum of c can be associated with the change in the level of availability of global information about the network structure. Therefore, although the shortest path lengths are required to compute the transition probabilities in the implementation, we regarded bRW with an intermediate to low range of c as an effective propagation strategy with respect to the information cost.

In Fig 3B, we show the elapsed time for transmitting 100 messages or sets of packets under bRW across the spectrum of the control parameter c. When c was relatively small, the elapsed time of packet switching was longer than that of message switching (e.g., $c = 0.01$, $p = 5.98 \times 10^{-34}$, FDR corrected, Cliff's delta $= 1$) as seen in the case with RW. When c was relatively large on the other hand, no significant difference was observed between the elapsed times of message switching and packet switching (e.g., $c = 10$, $p = 0.923$, FDR corrected, Cliff's delta $= -0.014$) as in the case with SP. The elapsed time of packet switching was shorter than that of message switching when c was specified within an intermediate range (e.g., $c = 0.7$, $p = 2.35 \times 10^{-8}$, FDR corrected, Cliff's delta $= -0.463$; $c = 1$, $p = 1.29 \times 10^{-9}$, FDR corrected, Cliff's delta $= -0.504$). In this range, the speed of network communication was high and comparable to the speed under SP. These results also suggest that packetization improves communication efficiency in brain networks with rapid and cost-effective propagation strategies.

We further confirmed that the results of the elapsed time comparison were robust against various changes applied to the default simulation settings. We describe these modified simulation settings and show the results obtained with them in **Supplementary results** and **Supplementary figures**.

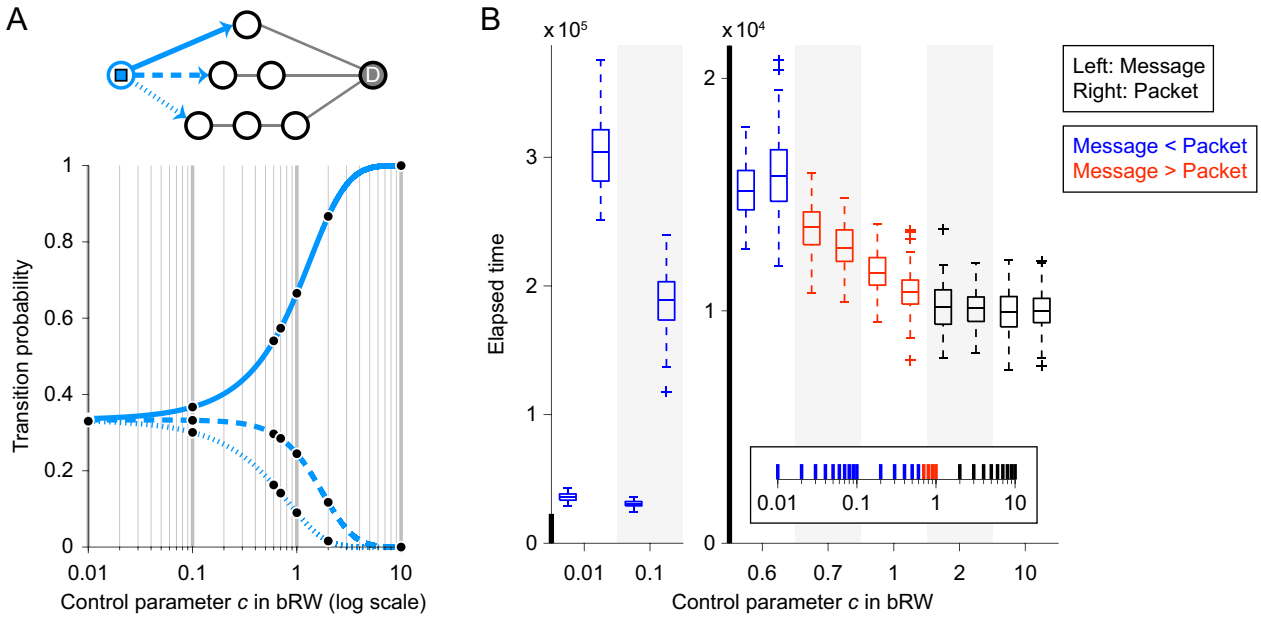

Fig 3 Simulations with the biased random walk (bRW) strategy. (A) Transition probability to neighboring nodes in a toy example case under bRW over the spectrum of the control parameter c. The transition probabilities are shown for the message or packet at the leftmost node (in the network shown above the plot) that has three neighboring nodes whose shortest path lengths to the destination node D are one (top), two (middle), and three (bottom). The line types of the arrows toward the neighboring nodes correspond to the line types in the plots of the transition probabilities. The black dots in the plot indicate the transition probabilities at c for which the distributions of the elapsed time are shown in panel B. (B) Elapsed time for transmitting 100 messages or sets of packets under bRW over the spectrum of c. The boxplots are colored in the same manner as in Fig 2B (blue: longer elapsed time of packet switching; red: shorter elapsed time of packet switching; black: no elapsed time difference between message switching and packet switching) ($p < 0.05$, FDR corrected for the 28 comparisons at $c \in \{0.01, 0.02, \ldots, 0.09, 0.1, 0.2, \ldots, 0.9, 1, 2, \ldots, 9, 10\}$). See the inset located at the bottom right for statistical results at all the considered values of c.

Node-wise metrics of communication dynamics

So far, we have demonstrated that the results of whether packetization improved the communication efficiency in the brain network differed across the propagation strategies used in the simulations. In this section, we investigate its reason by computing node-wise metrics derived from the simulated communication dynamics. Here we employed communication metrics used in the previous studies [20, 21]: the proportion of time that a node was busy (*utilization*) and the mean number of signals (messages or packets) at a node (*node contents*) (see **Materials and methods** for their formal definitions). To properly compare the node contents between message switching and packet switching, we divided the original node contents metric by the total capacity of a node (= the maximum buffer size plus one) for normalization.

Fig 4 presents the relations between the communication metrics and the in-degree (the number of

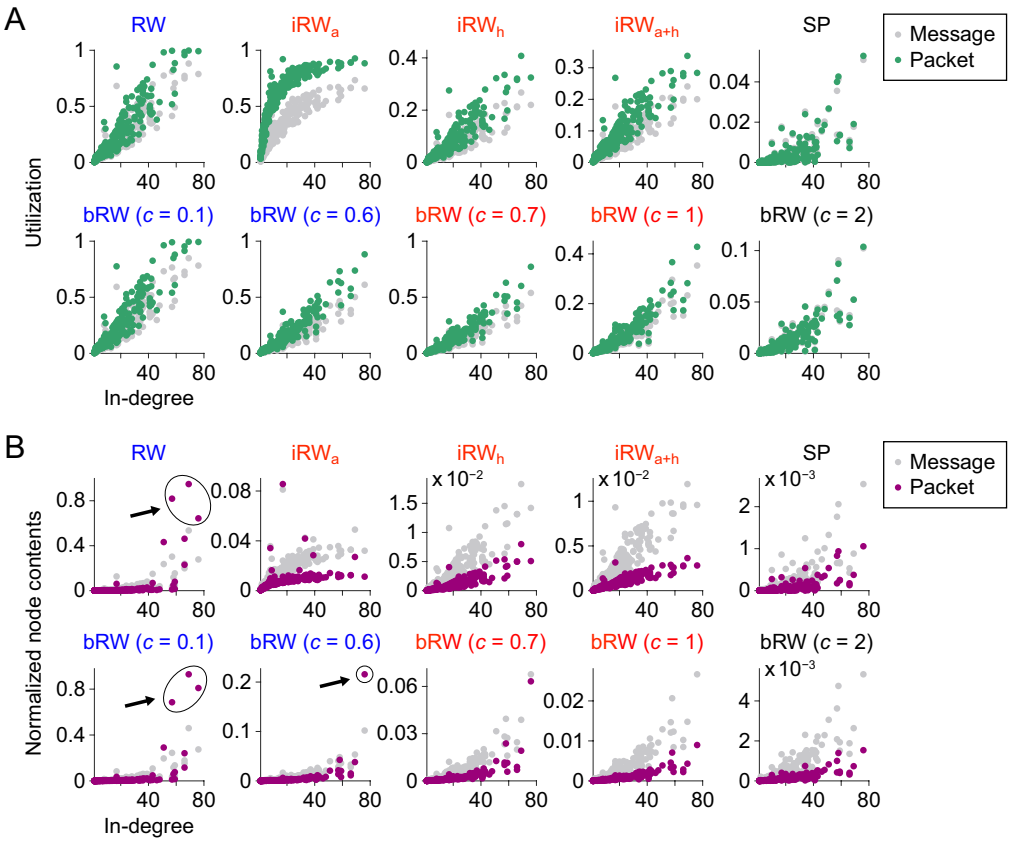

Fig 4 Node-wise metrics of simulated communication dynamics. (A) Relation between utilization and in-degree (each dot represents a node). Utilization was averaged over 100 simulation samples. Scatter plots for message switching (gray) and packet switching (green) are presented for each propagation strategy. The text color of each strategy corresponds to the color of the boxplots in Figs 2B and 3B. (B) Relation between normalized node contents and in-degree. Normalized node contents were averaged over 100 simulation samples. Arrows and ellipses in the scatter plots indicate several high in-degree nodes whose normalized node contents for packet switching (purple) were around twice as large as those for message switching (gray).

incoming connections; see Fig 1A) of the brain network used in the simulations. In SP and bRW with $c = 2$, utilization was almost identical between message switching and packet switching, which would explain why the elapsed times of both switching architectures were essentially the same under these propagation strategies. In iRW and bRW with $c = 0.7$ and $c = 1$, utilization was greater and normalized node contents were smaller for packet switching in most nodes, indicating that packets more diversely propagated across the network compared to messages. This result suggests that packetization allowed utilizing the whole network more efficiently and shortened the elapsed time with these propagation strategies. In RW and bRW with $c = 0.1$ and $c = 0.6$, normalized node contents for packet switching were around twice as large as those for message switching in a few high in-degree nodes indicated by arrows and ellipses in Fig 4B. These hub nodes that gathered many packets were areas 23c, 32, and 46 in the macaque brain network.

At these nodes, utilization for packet switching was close to 1 (i.e., they were always occupied by packets) under RW and bRW with $c = 0.1$. These results indicate that a few hub nodes played the bottleneck role and slowed down packet-based communication with these propagation strategies.

Simulations using randomized networks

To further investigate the role of hub nodes in the communication dynamics, we ran simulations on networks constructed by randomly rewiring connections in the original brain network. We employed randomized networks in which rewiring was constrained to preserve the in-degree and out-degree (the numbers of incoming and outgoing connections) of nodes in the original brain network (Fig 5A; hub nodes remained) and those in which connections were fully rewired (Fig 5B; no hub nodes existed).

Fig 5C shows the elapsed time for transmitting 100 messages or sets of packets in the simulations using the degree-preserved randomized networks. With these randomized networks, essentially the same results were observed as in the simulations with the original brain network (Figs 2B and 3B). By contrast, when the fully randomized networks were used in the simulations, packetization shortened the elapsed time not only for iRW and bRW with $c = 1$ but also for RW and bRW with $c = 0.1$ and $c = 0.01$ (Fig 5D). Nodes acting as bottlenecks under RW disappeared, where no node with packet switching exhibited a utilization close to one (Fig 5F, top) or nearly twice the normalized node contents compared to message switching (Fig 5F, bottom), unlike in the simulations using the original brain network (Fig 4) and the degree-preserved randomized networks (Fig 5E). These results suggest that the existence of hub nodes in the brain network was a reason why packetization slowed down the network communication under RW and bRW with a small c.

Discussion

To evaluate the plausibility of message switching and packet switching as a building block of brain network communication models, we examined whether or not packetization improves the communication efficiency in brain networks with rapid and cost-effective propagation strategies. To this end, we performed discrete-event simulations of the communication dynamics in a macaque brain network and compared the elapsed times to transmit signals from source to destination nodes between message switching and packet switching. We found that the elapsed time was shorter for packet switching than message switching under the informed and biased versions of RW that balanced communication speed and information cost. This finding indicates that packetization of signals allows for faster and more efficient communication in brain networks with physiologically plausible propagation strategies, strengthening the plausibility of packet switching for brain network communication models. We then explored the reason why the speed gain from packetization depended on the propagation strategies used in the simulations. By calculating communication metrics

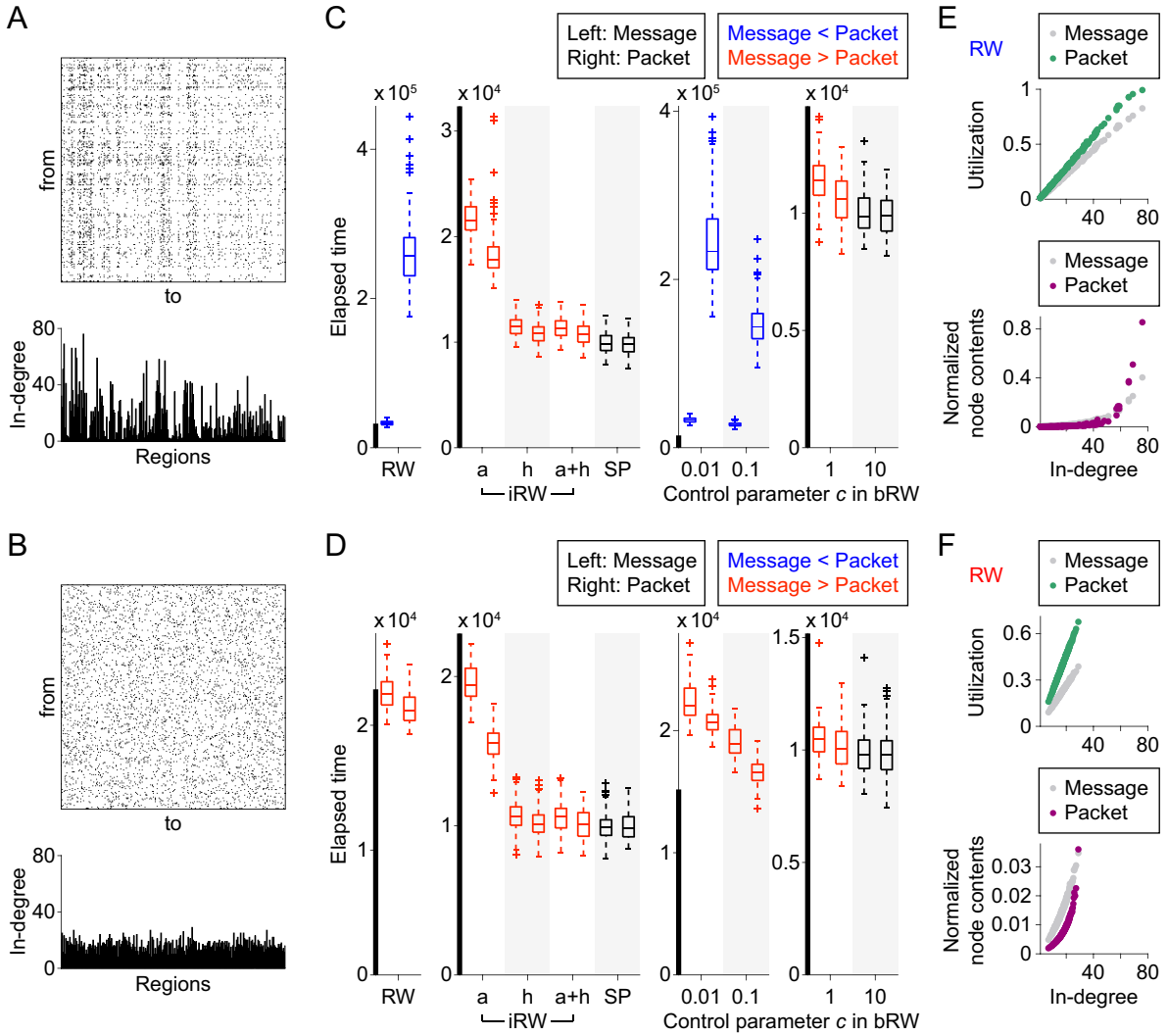

Fig 5 Results of simulations using randomized networks. (A) Adjacency matrix (top) and in-degree (bottom) of a degree-preserved randomized network. (B) Adjacency matrix (top) and in-degree (bottom) of a fully randomized network. (C) Elapsed time for transmitting 100 messages or sets of packets in the simulations using the degree-preserved randomized networks. (D) Elapsed time for transmitting 100 messages or sets of packets in the simulations using the fully randomized networks. The boxplots in panels C and D are colored in the same manner as in Figs 2B and 3B. (E) Relation between utilization (top) or normalized node contents (bottom) and in-degree, derived from 100 samples of the degree-preserved randomized networks. The metrics were averaged over all samples. (F) Relation between utilization (top) or normalized node contents (bottom) and in-degree, derived from 100 samples of the fully randomized networks. When averaging the metrics, nodes were sorted in an ascending order of their in-degrees.

and performing randomized network analysis, we demonstrated that the existence of hub nodes in brain networks plays a key role in differentiating between the propagation strategies for which packetization speeds up or slows down the transmission of signals in brain networks.

The results in this study support the idea that packet switching is more plausible than message switching as a switching architecture of brain network communication models [29]. The plausibility of switching architectures for brain networks has not been investigated in such depth as propagation strategies [23–25], except for the theoretical assessments by Graham and Rockmore [29]. Our study has provided empirical simulation results to advance the discussion about plausible switching architectures for brain networks. Regarding propagation strategies, it has been considered reasonable to adopt a strategy that balances communication speed and information cost in brain network communication models [23–25]. Here we demonstrated that, under such physiologically plausible propagation strategies, packet switching achieved faster communication in a macaque brain network compared to message switching. Communication being faster is just one criterion; however, this finding reinforced the validity of the use of packet switching for building communication models in brain networks. As the static structure of brain networks has a characteristic topology that speeds up communication between distant cortical regions [37], the dynamic switching architecture could also be designed to allow for faster communication through the packetization of cortical signals in brain networks.

If cortical signals in brain networks are exchanged among regions in the manner of packet switching, our results also strengthened the validity of the use of propagation strategies that balance communication speed and information cost for building brain network communication models. Prior to the present study, packet switching was thought of as a physiologically plausible type of switching architecture [20], as it has advantages in network communication (for instance, its ability to reroute network traffic and its efficiency in sparse communication systems [29, 31]) and, moreover, previous neurophysiological studies reported findings indicating packet-based communication in the cortex [32]. We demonstrated that only rapid and cost-effective propagation strategies achieved faster brain network communication with packet switching than message switching. In contrast, slow propagation strategies such as RW were particularly unsuitable for packet switching as we observed that packetization of cortical signals in the simulations significantly slowed down the speed of interregional communication. Taken together, our findings support the plausibility of using rapid and cost-effective strategies and packet switching as the propagation strategy and switching architecture of brain network communication models.

Why did packetization of cortical signals in brain networks achieve faster communication only under propagation strategies that balance communication speed and information cost? One potential reason is that such balanced strategies allowed packet switching to maximize its advantages. For the balanced strategies, the higher communication speed reduced the signal density in the network and, in turn, maintained the efficiency of packet switching [29, 31]. At the same time, the lower information cost generated randomness in the propagation behavior, and as a result, packetization allowed more edges in the network to be utilized on average. Another reason may come from the fact that structural brain networks have several high-degree hub nodes [38, 39]. These hubs played the bottleneck role under low-speed propagation strategies (e.g., RW),

and packetization did not improve the communication efficiency in this case but rather worsened it. As RW slowed down communication also in the simulations using degree-preserved randomized networks, this property can be generalized for many other networks in which high-degree hubs exist [40, 41]. Therefore, propagation strategies taking the speed into account would be necessary for packet-based communication in arbitrary networks containing hub nodes.

This study is subject to several methodological limitations. Firstly, since the mechanism of how cortical areas communicate throughout the whole brain network remains elusive, we simplified the communication dynamics in the simulation models as much as possible, especially regarding the dynamics of packet-based communication. For instance, packets were simply assumed to flow individually over the network; however, we could also hypothesize that packets in the same message take the same route toward the destination node. In fact, we have reached the same conclusion even with this alternative hypothesis (see **??**), indicating that the results were robust against variations in the modeling of packet-based communication. Secondly, we evaluated the communication efficiency when comparing message switching and packet switching but did not assess other aspects of communication. For example, the costs of splitting a message at a source node and merging packets at a destination node were ignored in the comparison due to the simplification of the simulation models. Finally, we did not use propagation strategies other than RW, SP, and their intermediates in terms of communication speed and information cost (iRW and bRW) in simulations. We assumed a single propagation strategy for all communication processes in a simulation sample, while there is a possibility that neural systems might combine aspects of RW and SP [23, 42]. We could not examine the navigation strategy [24] as it needs the location information of all nodes for signal propagation, whereas the coordinates of several nodes are not available for the hbrain network used in this study. We also did not investigate the broadcasting strategy [22] since signals multiply over time by broadcasting and this property makes it difficult to compare the results with those obtained from walk-based propagation strategies (e.g., RW and SP).

The current study is a first step toward a comprehensive evaluation of the validity of approximations applied to communication models in brain networks. Demonstrating the speed gain by packetization of signals with rapid and cost-effective propagation strategies in this study supported the plausibility of packet switching as a building block of brain network communication models; however, this evaluation approach was rather indirect. Our next step is to assess the validity and plausibility in a more direct manner using real experimental data. A promising approach is to calculate the similarity of resting-state functional connectivity in empirical brain activity data [13–15] and edgewise metrics quantifying the frequency of communication between cortical regions in simulations [20]. By computing such a metric from the communication dynamics simulated for a combination of switching architecture and propagation strategy, and then comparing it to empirical functional connectivity, we could quantify how well each combination of model approximations can explain functional interactions among cortical regions in empirical data [43]. We plan to start this

direction of future research using a human connectome dataset [44] from which we can construct structural and functional connectivity networks in the human brain.

In conclusion, we demonstrated that packetization of cortical signals speeds up communication in brain networks simulated with rapid and cost-effective propagation strategies. This result supports the plausibility of packet switching as a building block of brain network communication models. Future studies are required to further examine the plausibility of packet switching by comparing edgewise metrics derived from simulated communication dynamics and functional connectivity obtained from empirical brain activity data.

Materials and methods

Brain network data

The brain network employed in this study was derived from the CoCoMac database [1, 35] that provides white matter structural connectivity information of the macaque brain reported in existing tract tracing studies. The connectivity data was originally made by querying this database [36] and later refined to obtain a fully connected brain network [34]. This brain network, which was used in simulations of the cortical communication dynamics in previous [20, 21] and present studies, was comprised of 242 cortical regions (nodes) and $4,090$ directed connections (edges) represented in binary format (connection present $= 1$ and absent $= 0$) and contained no self-connections (see Fig 1A).

Discrete-event simulation

We simulated the communication dynamics in the macaque brain network using discrete-event simulation techniques [20, 21, 33]. In simulations with message switching, individual signals (messages) were generated in the network as a Poisson process with exponentially distributed inter-arrival times (arrival rate $\lambda = 0.01$) [20, 21]. To each message, a pair of source and destination nodes were randomly assigned. A message was transmitted to one of the neighboring nodes under a given propagation strategy until it reached its destination node. After reaching the destination node, the message was removed from the network. The time that a message spent at each node (service time) was exponentially distributed (service rate $\mu = 0.02$ in the default simulation setting of our simulations) [20, 21]. The ratio of the arrival rate to the service rate (λ/μ) governed the dynamics of the whole system and was specified so that the number of messages in the network did not monotonically increase during the simulations [20, 21]. If a message arrived at a node that was already occupied by another message, it was placed in a buffer and formed a queue. Messages entered the node on a LIFO basis [20, 21] and a maximum buffer size was imposed ($H = 20$) [20, 21] in the default setting. In this case, a message arriving at a fully occupied buffer caused the oldest message in the queue to be ejected and removed from the network. The state of the system was updated at non-uniform

intervals because of the presence of stochastic variables in inter-arrival times and service times. Fig 1B shows a schematic description of the discrete-event simulation with message switching.

In simulations with packet switching, the entire message was split into smaller packets when being transmitted to neighboring nodes. A message was divided into $n = 5$ equally sized packets in the default setting. A set of n packets was generated at the source node and transmitted to neighboring nodes under a given propagation strategy toward their common destination node. Packets in the same message individually propagated over the network in the default setting, such that they could take different routes and arrive at the destination node with different propagation delays. The service rate and the maximum number of slots in a buffer for a packet were specified as $n\mu$ and nH, respectively (see Fig 1C).

Comparison of communication efficiency

To examine whether packetization speeds up or slows down the communication over the brain network, we compared the communication efficiency between message switching and packet switching. We evaluated the communication efficiency by measuring the elapsed time in the discrete-event simulation to transmit 100 messages or their corresponding sets of packets to their destination nodes in the brain network (the shorter the elapsed time is, the higher the communication efficiency is). The elapsed time of message switching was defined as the duration from when the first message was generated at a source node until when 100 messages in total arrived at their respective destination nodes. The elapsed time of packet switching was the duration from when the first set of packets was generated at a source node until when all n packets in 100 sets of packets arrived at their respective destination nodes. We ran 100 simulations each for message switching and packet switching. Using these simulation samples, we examined whether the elapsed time of packet switching was shorter or longer than that of message switching for each of the propagation strategies described in the next subsection.

Propagation strategies

We compared the communication efficiency between message switching and packet switching under the following strategies of signal propagation in networks: random walk (RW), shortest path (SP), and informed and biased versions of RW (iRW and bRW) that have intermediate properties between RW and SP in terms of communication speed and information cost.

In RW, a message or packet was randomly transmitted to one of the neighboring nodes of the current node with an equal probability. In this strategy, no global information about the network structure was required for signal propagation. RW was used in the previous implementations of discrete-event simulation for brain networks [20, 21].

On the other hand, a message or packet in SP was transmitted along the shortest path between the source and destination nodes. When there were multiple shortest paths, a message or packet was randomly

transmitted with an equal probability to one of the neighboring nodes that were closest to the destination node in terms of the shortest path length. For signal propagation with this strategy, full connectivity information of the network was necessary to determine the shortest path. Propagation with SP has been assumed in the definitions of several network metrics, e.g., global efficiency [27, 45].

The iRW strategy uses local information only from neighboring nodes. We implemented three different versions of iRW (Fig 2A): (1) iRW with a rule of avoiding busy nodes ($\mathrm{iRW_a}$), (2) iRW with a rule of directly hopping to the destination node if it is one of the neighboring nodes ($\mathrm{iRW_h}$), and (3) iRW with both of these two rules ($\mathrm{iRW_{a+h}}$). In $\mathrm{iRW_a}$ and $\mathrm{iRW_{a+h}}$, a message or packet was transmitted to an unoccupied neighboring node when it existed. When such a node did not exist, a message or packet was transmitted to a neighboring node with the minimum queue length in the buffer. When there were multiple candidate nodes to transmit a message or packet, one of them was randomly selected with an equal probability. In $\mathrm{iRW_h}$ and $\mathrm{iRW_{a+h}}$, a message or packet was deterministically transmitted to the destination node if it was included in the set of the neighboring nodes to the current node.

The bRW strategy [25] can exhibit the propagation behavior between RW and SP. In bRW, the probability that a message or packet was transmitted from the current node i to one of its neighboring nodes j was defined as

$$p_{ijd} = \exp(-(c(l_{ij} + g_{jd}) + l_{ij}))\frac{1}{Z_{id}}, \tag{1}$$

where d is the destination node of the message or packet, c is the control parameter, l_{ij} is the length of the edge connecting nodes i and j (or $l_{ij} = \infty$ if this connection is absent), g_{jd} is the shortest path length between node j and destination d, and $Z_{id} = \sum_j \exp(-(c(l_{ij} + g_{jd}) + l_{ij}))$ is a normalization factor. As the brain network used in this study was a binary network and distance information was not available for all edges, we specified all edge lengths as $l_{ij} = 1$. The term $l_{ij} + g_{jd}$ denotes the minimum distance in hops between node i and destination d via neighboring node j. The control parameter c can change the extent to which the global information about the network structure was available for signal propagation (see Fig 3A for how c changed the transition probability in a toy example case). If $c = 0$, the transition probability p_{ijd} was reduced to that of RW as p_{ijd} became the same across all neighboring nodes when $l_{ij} = 1$. If $c \to \infty$, on the other hand, p_{ijd} was reduced to that of SP as $p_{ijd} \to 1$ at a neighboring node j for which $l_{ij} + g_{jd}$ was the minimum (i.e., j closest to d in terms of the shortest path length). When there were more than one such neighboring node due to the existence of multiple shortest paths, $p_{ijd} \to 1/$the number of those nodes.

Communication metrics

From the simulated communication dynamics in the brain network, we calculated two node-wise metrics: the proportion of the time that a node was busy (*utilization*) and the mean number of messages or packets at a node (*node contents*) [20, 21]. These metrics were derived from the following simulation variables for

node i at time t: the server contents $s_i(t) \in \{0, 1\}$, which represents whether there is a message or packet currently in service ($s_i(t) = 1$) or not ($s_i(t) = 0$), and the queue length $q_i(t) \in \{0, \ldots, H\}$ (H: the maximum buffer size), which represents the number of messages or packets in the buffer. The utilization of node i was defined as the proportion of simulation time having $s_i(t) = 1$. The node contents were defined as the sum of the server and queue contents, $n_i(t) = s_i(t) + q_i(t)$. In **Results**, we show the normalized version of node contents $n_i(t)/(1 + H)$ to properly compare this metric between message switching and packet switching.

Randomized networks

To explore the influences of hub nodes on the simulated communication dynamics, we replaced the original brain network in the simulations with two types of randomized networks generated by rewiring pairs of edges in the original network. We considered i) degree-preserved randomized networks in which edges were rewired while preserving the sequences of the in-degree and out-degree of nodes in the original network and ii) fully randomized networks in which edges were rewired with no constraint. We generated 100 different realizations of the degree-preserved or fully randomized networks to obtain the distributions of the elapsed time in Fig 5C or D. The same sets of the 100 randomized networks were used in the simulations for each combination of the propagation strategies and switching architectures.

Acknowledgements

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References

[1] Stephan KE, Kamper L, Bozkurt A, Burns GAPC, Young MP, Kötter R. Advanced database methodology for the Collation of Connectivity data on the Macaque brain (CoCoMac). Philos Trans R Soc Lond B Biol Sci. 2001; 356: 1159–1186.

[2] Hagmann P, Cammoun L, Gigandet X, Meuli R, Honey CJ, Wedeen VJ, et al. Mapping the structural core of human cerebral cortex. PLOS Biol. 2008; 6: e159.

[3] Markov NT, Ercsey-Ravasz MM, Ribeiro Gomes AR, Lamy C, Magrou L, Vezoli J, et al. A weighted and directed interareal connectivity matrix for macaque cerebral cortex. Cereb Cortex. 2014; 24: 17–36.

[4] Oh SW, Harris JA, Ng L, Winslow B, Cain N, Mihalas S, et al. A mesoscale connectome of the mouse brain. Nature. 2014; 508: 207–214.

[5] van den Heuvel MP, Bullmore ET, Sporns O. Comparative connectomics. Trends Cogn Sci. 2016; 20: 345–361.

[6] Breakspear M. Dynamic models of large-scale brain activity. Nat Neurosci. 2017; 20: 340–352.

[7] Honey CJ, Kötter R, Breakspear M, Sporns O. Network structure of cerebral cortex shapes functional connectivity on multiple time scales. Proc Natl Acad Sci U S A. 2007; 104: 10240–10245.

[8] Honey CJ, Sporns O, Cammoun L, Gigandet X, Thiran JP, Meuli R, et al. Predicting human resting-state functional connectivity from structural connectivity. Proc Natl Acad Sci U S A. 2009; 106: 2035–2040.

[9] Cabral J, Hugues E, Sporns O, Deco G. Role of local network oscillations in resting-state functional connectivity. NeuroImage. 2011; 57: 130–139.

[10] Deco G, Jirsa VK. Ongoing cortical activity at rest: criticality, multistability, and ghost attractors. J Neurosci. 2012; 32: 3366–3375.

[11] Deco G, Cabral J, Woolrich MW, Stevner ABA, van Hartevelt TJ, Kringelbach ML. Single or multiple frequency generators in on-going brain activity: a mechanistic whole-brain model of empirical MEG data. NeuroImage. 2017; 152: 538–550.

[12] Fukushima M, Sporns O. Comparison of fluctuations in global network topology of modeled and empirical brain functional connectivity. PLOS Comput Biol. 2018; 14: e1006497.

[13] Fox MD, Snyder AZ, Vincent JL, Corbetta M, Van Essen DC, Raichle ME. The human brain is intrinsically organized into dynamic, anticorrelated functional networks. Proc Natl Acad Sci U S A. 2005; 102: 9673–9678.

[14] Damoiseaux JS, Rombouts SARB, Barkhof F, Scheltens P, Stam CJ, Smith SM, et al. Consistent resting-state networks across healthy subjects. Proc Natl Acad Sci U S A. 2006; 103: 13848–13853.

[15] Yeo BTT, Krienen FM, Sepulcre J, Sabuncu MR, Lashkari D, Hollinshead M, et al. The organization of the human cerebral cortex estimated by intrinsic functional connectivity. J Neurophysiol. 2011; 106: 1125–1165.

[16] Cabral J, Kringelbach ML, Deco G. Functional connectivity dynamically evolves on multiple time-scales over a static structural connectome: models and mechanisms. NeuroImage. 2017; 160: 84–96.

[17] Crofts JJ, Higham DJ. A weighted communicability measure applied to complex brain networks. J R Soc Interface. 2009; 6: 411–414.

[18] Abdelnour F, Voss HU, Raj A. Network diffusion accurately models the relationship between structural and functional brain connectivity networks. NeuroImage. 2014; 90: 335–347.

[19] Goñi J, van den Heuvel MP, Avena-Koenigsberger A, Velez de Mendizabal N, Betzel RF, Griffa A, et al. Resting-brain functional connectivity predicted by analytic measures of network communication. Proc Natl Acad Sci U S A. 2014; 111: 833–838.

[20] Mišić B, Sporns O, McIntosh AR. Communication efficiency and congestion of signal traffic in large-scale brain networks. PLOS Comput Biol. 2014; 10: e1003427.

[21] Mišić B, Goñi J, Betzel RF, Sporns O, McIntosh AR. A network convergence zone in the hippocampus. PLOS Comput Biol. 2014; 10: e1003982.

[22] Mišić B, Betzel RF, Nematzadeh A, Goñi J, Griffa A, Hagmann P, et al. Cooperative and competitive spreading dynamics on the human connectome. Neuron. 2015; 86: 1518–1529.

[23] Avena-Koenigsberger A, Misic B, Sporns O. Communication dynamics in complex brain networks. Nat Rev Neurosci. 2018; 19: 17–33.

[24] Seguin C, van den Heuvel MP, Zalesky A. Navigation of brain networks. Proc Natl Acad Sci U S A. 2018; 115: 6297–6302.

[25] Avena-Koenigsberger A, Yan X, Kolchinsky A, van den Heuvel MP, Hagmann P, Sporns O. A spectrum of routing strategies for brain networks. PLOS Comput Biol. 2019; 15: e1006833.

[26] Bullmore ET, Sporns O. Complex brain networks: graph theoretical analysis of structural and functional systems. Nat Rev Neurosci. 2009; 10: 186–198.

[27] Rubinov M, Sporns O. Complex network measures of brain connectivity: uses and interpretations. NeuroImage. 2010; 52: 1059–1069.

[28] Delvenne JC, Yaliraki SN, Barahon M. Stability of graph communities across time scales. Proc Natl Acad Sci U S A. 2010; 107: 12755–12760.

[29] Graham D, Rockmore D. The packet switching brain. J Cogn Neurosci. 2011; 23: 267–269.

[30] Graham DJ. Routing in the brain. Front Comput Neurosci. 2014; 8: 44.

[31] Kleinrock L. Queueing systems, volume 2: computer applications. New York: Wiley-Interscience; 1976.

[32] Luczak A, McNaughton BL, Harris KD. Packet-based communication in the cortex. Nat Rev Neurosci. 2015; 16: 745–755.

[33] Banks J, Carson II JS. Discrete-event system simulation. New Jersey: Prentice-Hall; 1984.

[34] Harriger L, van den Heuvel MP, Sporns O. Rich club organization of macaque cerebral cortex and its role in network communication. PLOS ONE. 2012; 7: e46497.

[35] Kötter R. Online retrieval, processing, and visualization of primate connectivity data from the CoCoMac database. Neuroinformatics. 2004; 2: 127–144.

[36] Modha DS, Singh R. Network architecture of the long-distance pathways in the macaque brain. Proc Natl Acad Sci U S A. 2010; 107: 13485–13490.

[37] Bullmore ET, Sporns O. The economy of brain network organization. Nat Rev Neurosci. 2012; 13: 336–349.

[38] Sporns O, Honey CJ, Kötter R. Identification and classification of hubs in brain networks. PLOS ONE. 2007; 2: e1049.

[39] van den Heuvel MP, Sporns O. Network hubs in the human brain. Trends Cogn Sci. 2013; 17: 683–696.

[40] Albert R. Scale-free networks in cell biology. J Cell Sci. 2005; 118: 4947–4957.

[41] Clauset A, Shalizi CR, Newman MEJ. Power-law distributions in empirical data. SIAM Rev. 2009; 51: 661–703.

[42] Betzel RF, Faskowitz J, Mišić B, Sporns O, Seguin C. Multi-policy models of interregional communication in the human connectome. bioRxiv. 2022; doi: 10.1101/2022.05.08.490752.

[43] Seguin C, Tian Y, Zalesky A. Network communication models improve the behavioral and functional predictive utility of the human structural connectome. Netw Neurosci. 2020; 4: 980–1006.

[44] Van Essen DC, Smith SM, Barch DM, Behrens TEJ, Yacoub E, Ugurbil K for the WU-Minn HCP Consortium. The WU-Minn Human Connectome Project: an overview. NeuroImage. 2013; 80: 62–79.

[45] Latora V, Marchiori M. Efficient behavior of small-world networks. Phys Rev Lett. 2001; 87: 198701.

Supplementary results

To confirm the main conclusion of this study that packetization improves the communication efficiency in brain networks with rapid and cost-effective propagation strategies, we examined whether the results of the elapsed time comparison were robust against the following five changes applied to the default simulation settings.

(i) **No buffer size limitation**. We removed the buffer size limitation in the default setting. The results were almost identical to those obtained with the buffer size limitation (see Fig S1).

(ii) **Decrease/increase of the number of packets in a message**. We changed the default number of packets in a message n from five to three and ten. While the different values of n changed the elapsed time of packet switching, the main conclusion derived from the elapsed time comparison between message switching and packet switching held in both decreased and increased cases (see Figs S2 and S3).

(iii) **Decrease/increase of the arrival rate**. We changed the arrival rate λ from 0.01 in the default setting to 0.005 (less frequent signal generation) and 0.02 (more frequent signal generation), which are the minimum and the maximum arrival rates used in Mišić et al. [20]. As in this previous study, we kept the service rate μ unchanged because the system dynamics were dependent on the ratio λ/μ. Figs S4 and S5 show that the main conclusion held with both decreased and increased arrival rates, although packetization did not speed up communication with $\mathrm{iRW_a}$ when $\lambda = 0.02$. In that case, $\mathrm{iRW_a}$ was no longer a rapid propagation strategy as its elapsed times were much longer than those of SP. In bRW, the range of the control parameter c from which packetization improved the communication efficiency became smaller when $\lambda = 0.005$ and larger when $\lambda = 0.02$.

(iv) **Packets following their foremost packet**. We changed the default setting in which each packet can individually take its own route to another setting in which all packets in the same message follow the route taken by their foremost packet. While following the foremost packet shortened the elapsed time of packet switching with slow propagation strategies (e.g., RW), it did not alter the main conclusion of the comparison results (see Fig S6).

(v) **First-in-first-out (FIFO) queuing system**. We replaced the LIFO queuing system in the default setting with the FIFO queuing system. In FIFO, the oldest message or packet in the buffer at a node was to start its service first after the previously occupying message or packet finished its service at this node, and a message or packet was removed from the network when it arrived at a node whose buffer was fully occupied by other messages or packets. We confirmed that there were no essential differences in the obtained results between LIFO and FIFO (see Fig S7).

Supplementary figures

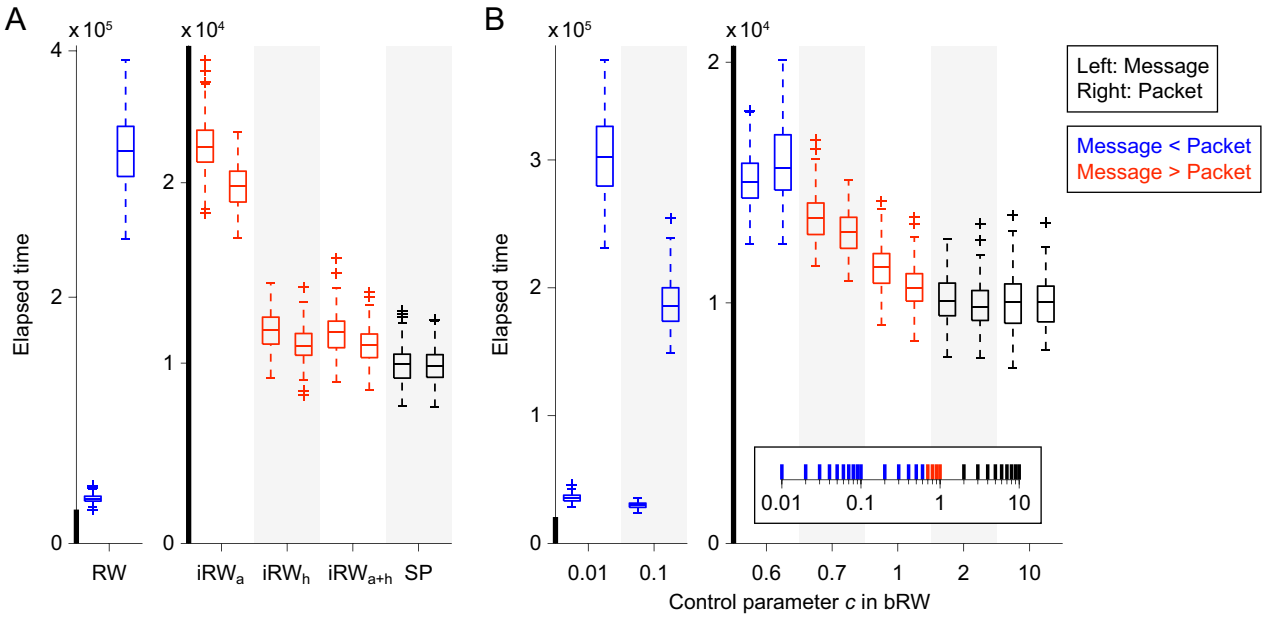

Fig S1 Elapsed time for transmitting 100 messages or sets of packets in the simulations with no buffer size limitation. (A) Elapsed time with RW, iRW, and SP. (B) Elapsed time with bRW. The boxplots are colored in the same manner as in Figs 2B and 3B.

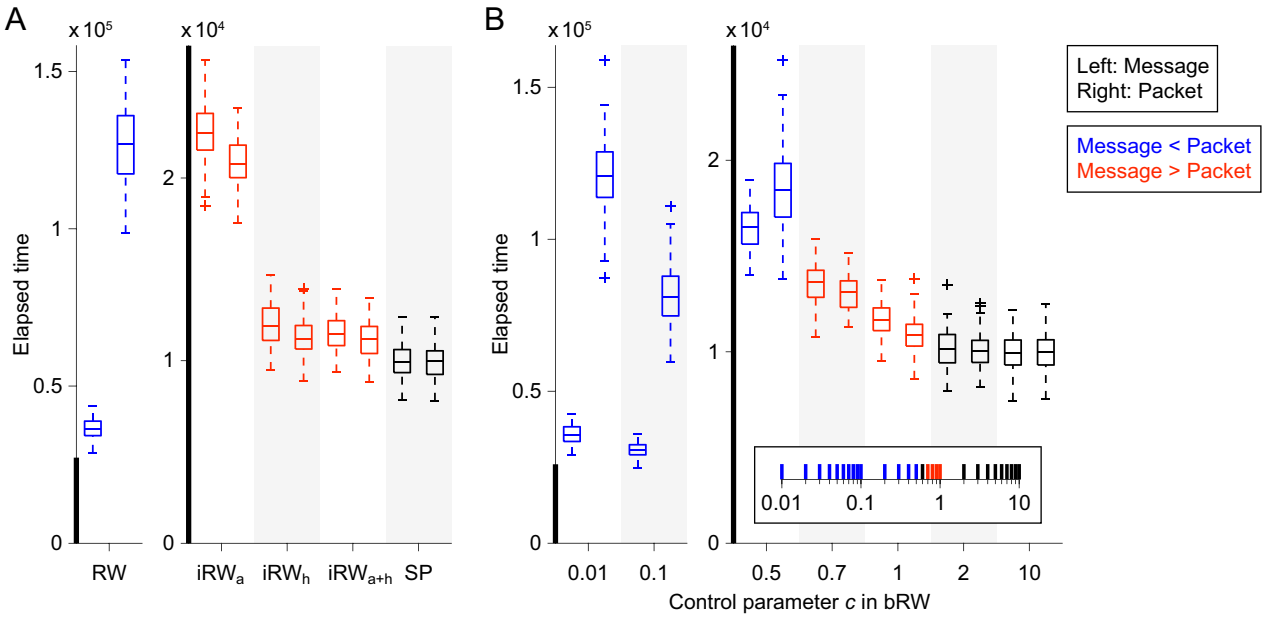

Fig S2 Elapsed time for transmitting 100 messages or sets of packets in the simulations with the number of packets in a message $n = 3$. (A) Elapsed time with RW, iRW, and SP. (B) Elapsed time with bRW.

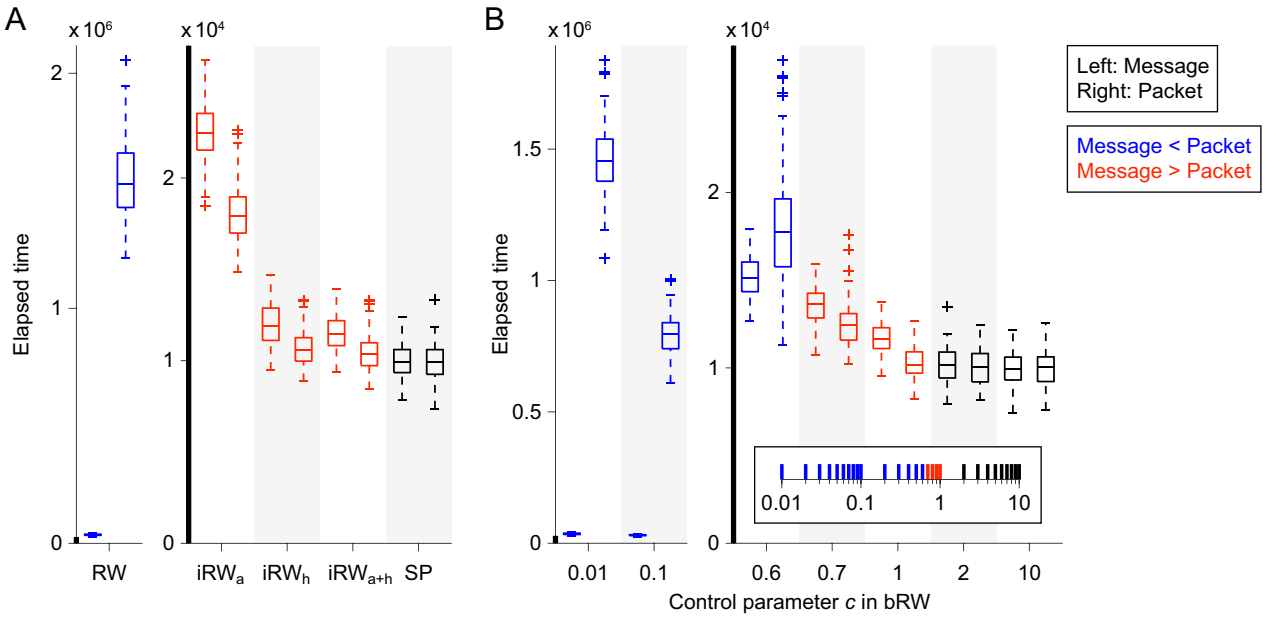

Fig S3 Elapsed time for transmitting 100 messages or sets of packets in the simulations with the number of packets in a message $n = 10$. (A) Elapsed time with RW, iRW, and SP. (B) Elapsed time with bRW.

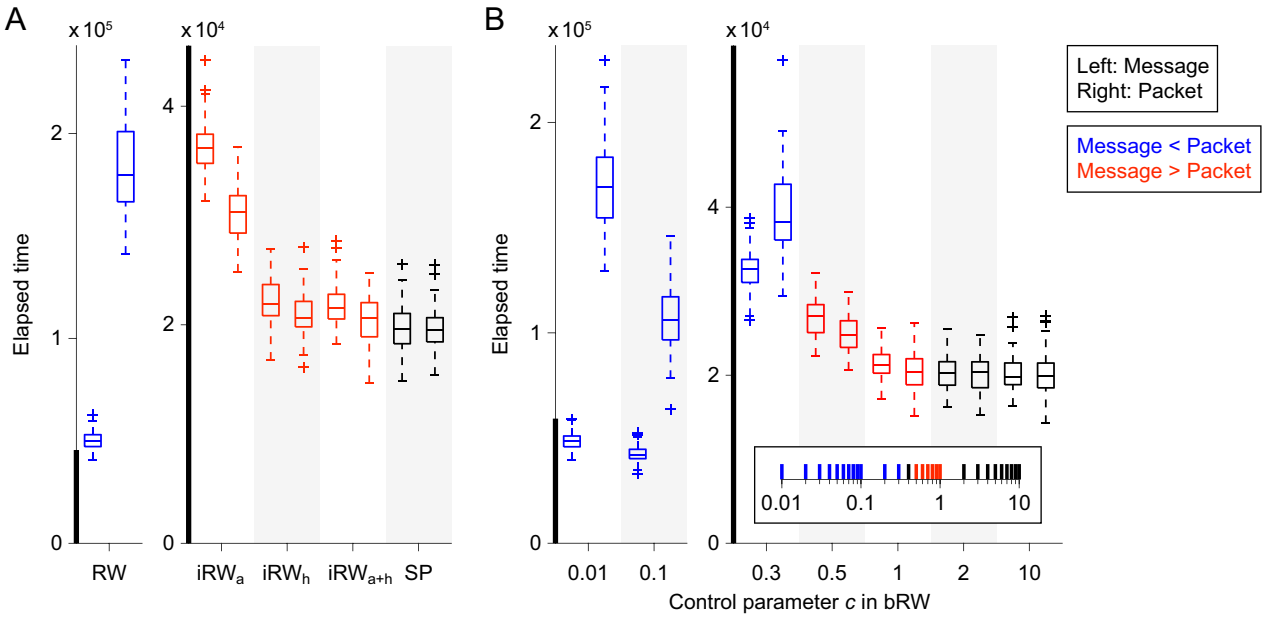

Fig S4 Elapsed time for transmitting 100 messages or sets of packets in the simulations with the arrival rate $\lambda = 0.005$. (A) Elapsed time with RW, iRW, and SP. (B) Elapsed time with bRW.

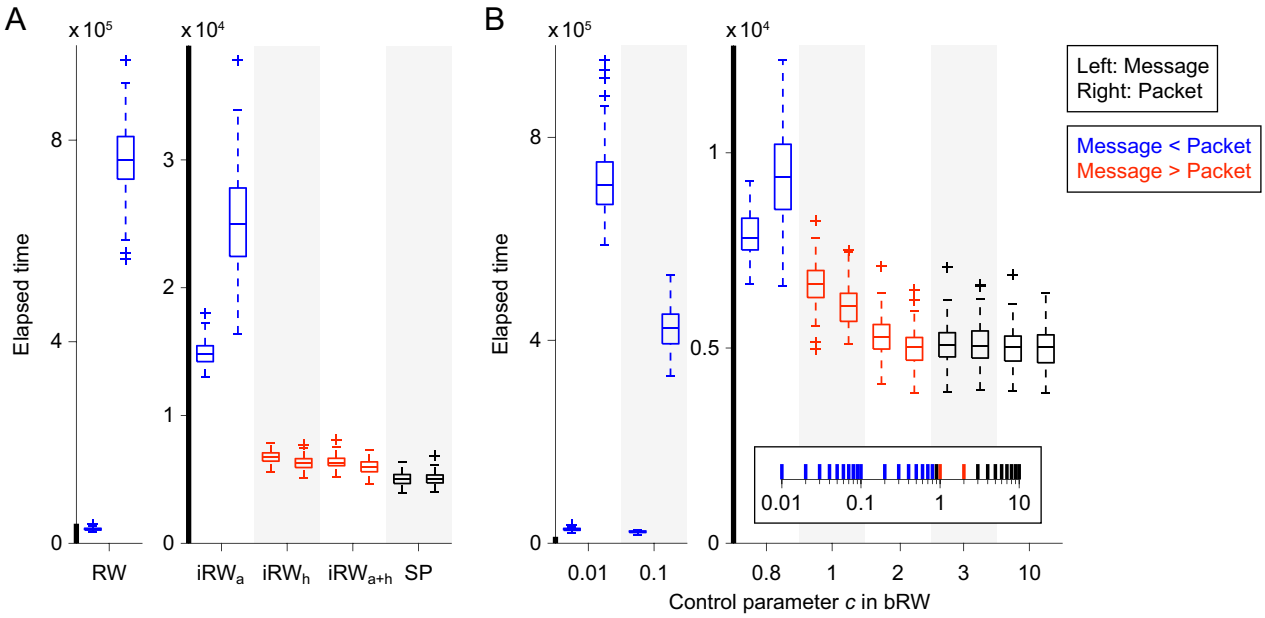

Fig S5 Elapsed time for transmitting 100 messages or sets of packets in the simulations with the arrival rate $\lambda = 0.02$. (A) Elapsed time with RW, iRW, and SP. (B) Elapsed time with bRW.

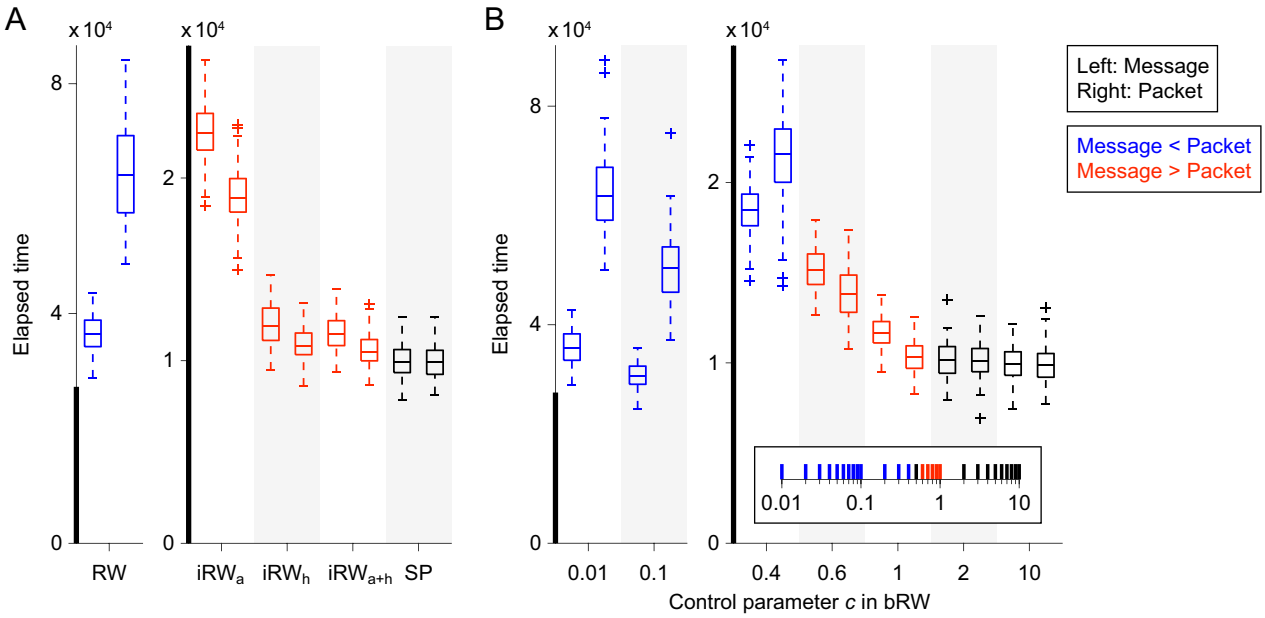

Fig S6 Elapsed time for transmitting 100 messages or sets of packets in the simulations when packets in a message follow the foremost packet. (A) Elapsed time with RW, iRW, and SP. (B) Elapsed time with bRW.

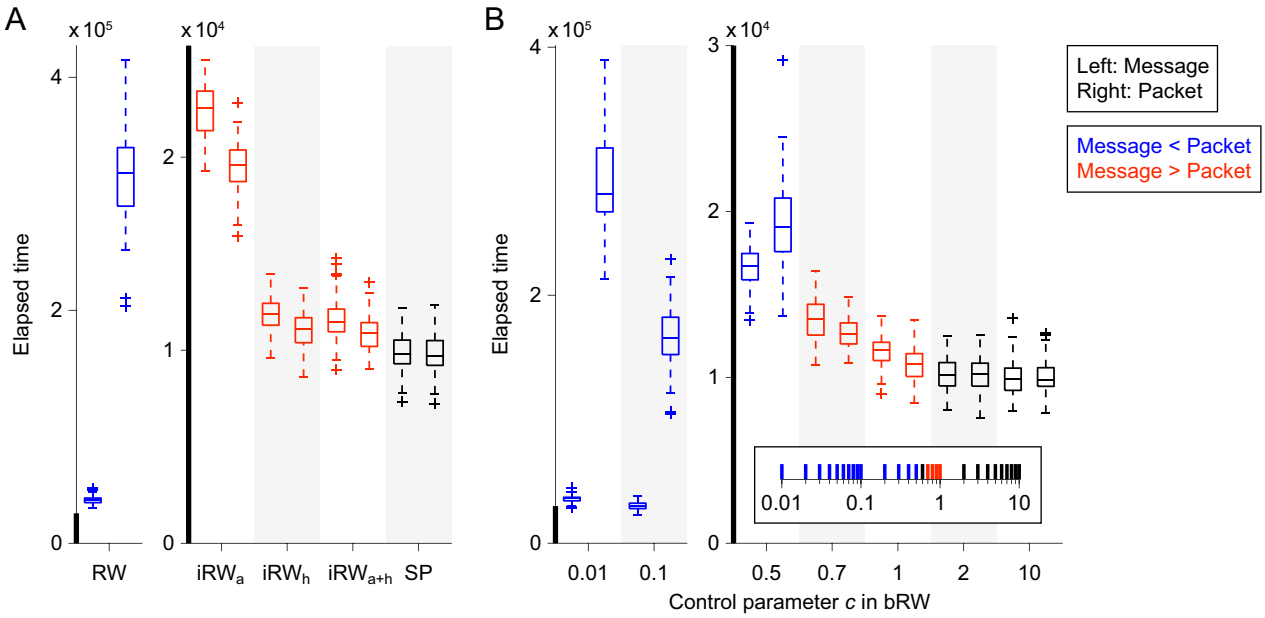

Fig S7 Elapsed time for transmitting 100 messages or sets of packets in the simulations with the FIFO queuing system. (A) Elapsed time with RW, iRW, and SP. (B) Elapsed time with bRW.