Random Hypergraph Models of Learning and Memory in Biomolecular Networks: Shorter-Term Adaptability vs. Longer-Term Persistency

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Abstract—Recent progress in genomics and proteomics makes it possible to understand the biological networks at the systems level. We aim to develop computational models of learning and memory inspired by the biomolecular networks embedded in their environment. One fundamental question is how the systems rapidly adapt to their changing environment in a short period (learning) while performing persistently through the longer time span (memory). We study this issue in a probabilistic hypergraph model called the hypernetworks. The hypernetwork architecture consists of a huge number of randomly sampled hyperedges, each corresponding to higher-order micromodules in the input. We find that a system consisting of a large number of a wide range of heterogeneous low-dimensional components has a fairly competitive chance of long-term survival (memory, persistency) and short-term performance (learning, adaptability) as opposed to a system consisting of a small number of high-dimensional, fine-tuned, complex components. Empirical evidence is offered to support these findings and theoretical explanations are given.

I. INTRODUCTION

Cells are highly complex information processing systems. Much progress has been made in elucidating the molecular mechanisms of individual cells during the last decades. In particular, recent progress in genomics and proteomics makes it possible to understand the biological units and processes at the systems level. These include gene regulation networks [7], metabolic pathways [5], signal transduction networks [2][8], and other protein interaction networks [9]. For example, Figure 1 shows an example regulatory network in a human cell [1], where a small number of genes interact more closely than others and the whole network builds an Internet-like hub structure.

These findings may shed light on the design principles of biological information processing systems which might be useful for building artificial information processing systems. For example, in contrast to the typical problem settings in machine learning, the biological learning systems are faced with continuous exposure to the environment. Simple organisms such as bacteria should strive to adapt to the changes in their resources of both beneficial (food) and harmful (poison) nature to swim and to survive [4]. Also, it is interesting to know how the biochemical networks maintain the stability while adapting to the cellular environmental changes. The life time of each molecule is very limited but the system or the population of the biomolecules maintains its robustness [14].

We aim to develop computational systems by mimicking the organizational and processing principles underlying the biomolecular networks. We ask the fundamental question of how the organisms adapt to the short-term environmental change (learning issue) while maintaining the longer-term persistency in performing a task (memory issue). Here we hypothesize that a key to the biological solution to this challenge is the diversity of the variety, size, and complexity of the molecular species and structures in the cell (and the organism). The biochemical signal transduction networks, for example, consist of various molecular species interacting with each other massively yet specifically [12]. The molecules are relatively simple, but their massive interaction in a network may exhibit complex, emergent behavior [2].

We use the random hypergraph models [6] to study the hypothesis that the diversity of the system in its organizational structure plays an important role in their adaptability in a short term and survivability in a long term. In Section II, we define the hypernetwork architecture. In Section III, we use the random graph process to build the hypernetwork structures that model the training data coming from the environment. The resulting network structures and their performances are examined in Section IV to study the relationship between the structural and functional properties. Section V summarizes the results and discusses future work.

II. THE HYPERNETWORK ARCHITECTURE

Hypernetworks are a generalization of the hypergraphs. A hypergraph is an undirected graph $G$ whose edges connect a non-null number of vertices [3], i.e. $G = (X, E)$, where $X = \{x_1, x_2, ..., x_n\}$, $E = \{E_1, E_2, ..., E_m\}$, and $E_i = \{x_{i_1}, x_{i_2}, ..., x_{i_k}\}$. $E_i$ is called the hyperedges. Mathematically, $E_i$ is a set and its cardinality (size) is $k \geq 1$, i.e., the hyperedges can connect more than two vertices while in ordinary graphs the edges connect up to two vertices, i.e., $k \leq 2$. A hyperedge of cardinality $k$ will be referred to as a $k$-hyperedge.

For example, a hypergraph may consist of seven vertices $X = \{x_1, x_2, ..., x_7\}$ and five hyperedges $E = \{E_1, E_2, E_3, E_4, E_5\}$ each having a different cardinality. A hypergraph can be represented as an incidence matrix. The incidence matrix of a hypergraph $G = (X, E)$ is a matrix $[a_{ij}]$ with $m$ rows that represent the hyperedges of $G$ and $n$
A hypernetwork is a hypergraph that is augmented with a weight value to each hyperedge (Figure 2). Formally, a hypernetwork \( H = (X, E, W) \) is a weighted hypergraph consisting of a set \( X \) of vertices, a set \( E \) of hyperedges, and a set \( W \) of weights. In contrast to ordinary graphs, a hypergraph consists of edges of cardinality \( 1 \leq k \leq n \), where \( n = |X| \). In this figure, each hyperedge \( E_i \) is represented as a polygon connecting the vertices in it. The thickness of each hyperedge is proportional to its weight \( w_j \).

For the hypernetwork model, \( x_{i_1}^{(n)} x_{i_2}^{(n)} ... x_{i_{|E_i|}}^{(n)} \) is a combination of \( k = |E_i| \) elements of the data item \( x^{(n)} \) which is represented as a \( k \)-hyperedge in the network.

Then, the probability of the data being generated from the hypernetwork is given as Gibbs distribution

\[
P(x^{(n)}|W) = \frac{1}{Z(W)} \exp \left\{ -E(x^{(n)}; W) \right\},
\]

where \( \exp \left\{ -E(x^{(n)}; W) \right\} \) is called the Boltzmann factor and the normalizing term \( Z(W) \) is expressed as

\[
Z(W) = \sum_{x^{(n)}} \sum_{E_i \in E} \prod_{j \in E_i} w_{i_1 i_2 ... i_{|E_i|}}^{(m)} x_{i_1}^{(m)} x_{i_2}^{(m)} ... x_{i_{|E_i|}}^{(m)},
\]

In effect, the hypernetwork represents a probabilistic model of the data set using a population of hyperedges and their weights.

It is interesting to note the relationship of the hypernetwork architecture and the traditional neural network or machine learning models. To see the connection, we define the potential function associated with the hyperedges as

\[
\Phi_{E_i}(x) = \prod_{x_j \in E_i} x_j = x_{i_1}, x_{i_2}, ..., x_{i_{|E_i|}},
\]

where \( k = |E_i| \) is the size of the \( i \)-th hyperedge. When the variables \( x_j \) are binary-valued, this potential function computes a logical conjunction of the variables. Using this potential function, the energy function can be expressed as

\[
E(x; W) = \sum_{i=1}^{|E|} w_{i_1 i_2 ... i_{|E_i|}} \Phi_{E_i}(x),
\]

which is a weighted sum of the potential functions. The weighting has a smoothing effect to make the logical decisions more robust [15]. If the \( x \)-variables take real values,
this results in a higher-order polynomial networks [18]. Thus
the hypernetwork structure in this case is a generalization of
the conventional polynomial networks where the degree and
order of the polynomials are arbitrary. Allowing only
\(k\)-hyperedges, the hypernetwork represents a polynomial
network of order \(k\).

The similarity to the multilayer perceptron is to be seen
by defining a sigmoid potential function, i.e.,

\[
\Phi_{E_i}(x) = \frac{1}{1 + \exp \left\{ - \sum_{x_j \in E_i} w_j x_j \right\}},
\]

where \(k_i = |E_i|\) is the size of receptive field of the sigmoid
unit. In general, different hyperedges have different \(k_i\) and \(k_i\)
is smaller than the number of inputs \(n\), i.e. \(k_i < n\), \(k_j < n\),
and \(k_i \neq k_j\) for most of \(i\) and \(j\). This heterogeneous
structure of the hypernetwork of sigmoid units is contrasted
with the conventional sigmoid neural networks where the
structure is homogeneous with a fixed receptive field size \(n\)
for all the neurons.

The hypernetwork can emulate the radial basis function
networks by defining a Gaussian potential function:

\[
\Phi_{E_i}(x) = \exp \left\{ - \frac{1}{\sigma_k} ||x^{(i)} - x||_{E_i} \right\},
\]

where \(||x^{(i)} - x||_{E_i} = \sum_{x_j \in E_i} x_j^{(i)} x_j\). Again, the hypernet-
work takes heterogeneous radial basis functions where the
dimension of the basis function is variable.

Figure 3 compares the output functions for the hyperedges
of different potential functions. Also shown is the effect of
the size of hyperedges. When the hyperedges are small,
\(i.e.\) for small \(k = |E_i|\), the receptive fields are narrow and
thus the hypernetwork builds a representation consisting of
low-dimensional, general components (micromodules). When
the hyperedges are large, the hypernetwork builds a
representation consisting of high-dimensional, specialized
components. To see the profile of distribution we consider the
histogram of the size of hyperedges. When the hyperedges are small,
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III. GENERATING RANDOM HYPERNETWORKS FROM DATA

For a \(k\)-hypergraph, the number of possible edges are

\[
|E| = C(n, k) = \frac{n!}{k!(n-k)!},
\]

where \(n = |X|\) and \(C(n, k)\) denotes the number of cases to
choose \(k\) elements from a population of \(n\) elements. If we
denote the set of all graphs as \(\Omega\), its size is

\[
|\Omega| = 2^{C(n, k)}.
\]

Since a hypernetwork is a multiset of hypergraphs, the size
of \(k\)-hypernetworks \(H^{(k)}\) is the multiples of \(|\Omega|\). For the class
of \((0, n)\)-hypernetworks, the number of possible hyperedges
is the multiples of

\[
|E| = \sum_{k=0}^{n} C(n, k) = \sum_{k=0}^{n} \frac{n!}{k!(n-k)!} = 2^n,
\]

and the size of the space of \((0, n)\)-hypernetworks is

\[
|\Omega| = 2^{2^n},
\]

where \(k\) is the maximum number of copies of an hyperedge
to appear in a hypernetwork.

We now introduce a stochastic method to search this
space. A random graph is a graph constructed by a random
procedure [6]. A random graph model chooses a graph at
random, with equal probabilities, from the set of all \(2^n\)
graphs whose vertex set is \([n] = \{1, 2, ..., n\}\). We consider a
probability space

\[
(\Omega, \mathcal{F}, \mathcal{P}),
\]

where \(\Omega\) is the set of all graphs with vertex set \([n]\), \(\mathcal{F}\) is the
family of all subsets of \(\Omega\), and to every \(\omega \in \Omega\) we assign its
probability as

\[
\mathcal{P}(\omega) = 2^{-C(n, k)},
\]

The probability space can be viewed as the product of
\(C(n, k)\) binary spaces. It is a result of \(C(n, k)\) independent
tosses of a fair coin, i.e. Bernoulli experiments.

The random hypernetworks can be generated by a binomial
random graph process. Given a real number \(p\), \(0 \leq p \leq 1\),
the binomial random (hyper)graph, denoted by \(G(n, p)\), is
defined by taking as \(\Omega\) the set of all hypergraphs on vertex
set \([n]\) and setting

\[
P(G) = p^{|E(G)|}(1-p)^{C(n,k)-|E(G)|},
\]

| Small \(k = |E|\) |
| Large \(k = |E|\) |
| Product | |
| Sigmoid | |
| Gaussian | |

Fig. 3. Three examples of potential (basis) functions to be associated with
the hyperedges. The potential functions with small \(k\)-hyperedges receive
inputs from a narrow range (in dimensions) while those with large \(k-
hyperedges observe a wide range of the input space. Thus, changing
the parameter \(k\) in the random hypernetworks has an effect of varying the
receptive-field size in neural networks.
where \(|E(G)|\) stands for the number of edges of \(G\). The hypernetworks are generated by repeating the random hypergraph process.

Alternatively, we can generate the random hypergraphs using a uniform random graph process. Given an integer \(M\), \(0 \leq p \leq C(n, k)\), the uniform random hypergraph, denoted by \(G(n, M, p)\), is defined by taking as \(\Omega\) the family of all graphs on the vertex set \([n]\) with exactly \(M\) edges, and as \(P\) the uniform probability on \(\Omega\),

\[
P(G) = C(C(n, k), M)^{-1},
\]

where \(G \in \Omega\). The hypernetworks are then generated by repeating the random hypergraph process. The binomial random graph model and the uniform random graph model are known to be asymptotically equivalent if \(C(n, k)p\) is close to \(M\) [6].

One difference in our approach from the typical random graph process is that we want to build a model of an environment rather than simply generate a random graph structure. This is where the role of training data \(D = \{x\}\) comes in. The basic idea is that, instead of inserting the structure of hyperedge, the random graph process inserts into the hypernetwork a hyperedge that is instantiated by the training sample. The whole procedure for building a \(k\)-hypernetwork that fits a given data set \(D\) is summarized as follows.

1. Start with the initial hypernetwork \(H = (X, E, W) = (\emptyset, \emptyset, \emptyset)\).
2. Get a training sample \(x \in D\). Generate a hypernetwork \(H' = (X', E', W')\) as follows:
   - Generate hyperedges (duplication permitted), \(E_i\), of cardinality \(k\) from \(x\) by a random hypergraph process.
   - \(E' = E' \cup \{E_i\}\).
   - \(W' = \{w | w = |E_i|, i = 1, \ldots, |E'|\}\).
   - \(X' = \{x_j | x_j \in E_i \in E'\}\).
3. \(H' = H \cup H'\).
4. Go to step 2 if not terminated.

The repeated application of the random graph process for the samples in the training set \(D\) results in resampling the training data onto the hypernetwork structure. When the problem is a supervised learning task, we can modify the random process to add an error correction procedure. It can be shown that this biased random process performs gradient search to find maximum-likelihood parameters for the training data set. To see this, given a set \(D = \{x^{(n)}\}_{n=1}^{N}\) of \(n\) independently and identically distributed examples, we consider the likelihood of the parameters \(W\):

\[
P(D|W) = \prod_{n=1}^{N} P(x^{(n)}|W),
\]

where \(P(x^{(n)}|W)\) has the form in Eqn. (2) and \(W\) consists of the weights or the number of copies of the hyperedges of size \(k\). Taking the logarithm of the likelihood we obtain

\[
\ln P(D|W) = \ln \prod_{n=1}^{N} P(x^{(n)}|W) = \sum_{n=1}^{N} \left[ \sum_{i_1, \ldots, i_{|E_i|}} w_{i_1 \ldots i_{|E_i|}} x^{(n)}_{i_1} \cdots x^{(n)}_{i_{|E_i|}} \right] - \ln Z(W).
\]

We take the derivative of the log-likelihood

\[
\nabla \ln \prod_{n=1}^{N} P(x^{(n)}|W) = \frac{\sum_{n=1}^{N} \left[ \sum_{i_1, \ldots, i_{|E_i|}} w_{i_1 \ldots i_{|E_i|}} x^{(n)}_{i_1} \cdots x^{(n)}_{i_{|E_i|}} \right]}{\ln Z(W)} \frac{\nabla \ln \prod_{n=1}^{N} P(x^{(n)}|W)}{\ln Z(W)}
\]

which leads to a learning rule (see [17] for derivation)

\[
N \left\{ \langle x_{i_1} \cdots x_{i_{|E_i|}} \rangle_{D\text{ata}} - \langle x_{i_1} \cdots x_{i_{|E_i|}} \rangle_{P(x|W)} \right\},
\]

where the two terms are defined as

\[
\langle x_{i_1} \cdots x_{i_{|E_i|}} \rangle_{D\text{ata}} = \frac{1}{N} \sum_{n=1}^{N} \left[ x^{(n)}_{i_1} \cdots x^{(n)}_{i_{|E_i|}} \right],
\]

\[
\langle x_{i_1} \cdots x_{i_{|E_i|}} \rangle_{P(x|W)} = \sum_{x} \left[ x_{i_1} \cdots x_{i_{|E_i|}} P(x|W) \right].
\]

Eqn. (20) suggests that maximum-likelihood is achieved by reducing the difference between the average frequencies of the hyperedges in the data set and in the hypernetwork model, as described above.

IV. ADAPTABILITY VS. PERSISTENCY

The random hypernetwork architecture is inspired by the complex, heterogeneous organization of biomolecular networks in nature. We are interested to understand and simulate the process by which a complex randomized system organizes itself to a structured system to perform a task persistently while adapting to be robust against temporary perturbations from the environment. For empirical study, here we use various data sets as a surrogate for the environment. These include 3760 digit images (of 64 bits each), 165 face images (480 bits), and 120 gene expression samples (12600 bits) [19]. The characteristics of these data sets interesting to us in this study is they represent highly noisy and corrupted environments. Based on the data we build hypernetworks by the procedure described in the previous section, and the structural and functional properties of the networks are examined to see what factors are crucial. In particular, we analyze the hypergrams to see the relationship between the diversity of the hyperedges and the performance of hypernetworks for a wide range of tasks.

We use the hypernetwork model consisting of hyperedges with simple product potential functions. The random graph process generates random subsets of variables whose values are sampled from the training data. The use of a large number of relatively simple yet heterogeneous hyperedges may test the potential role of diversity and flexibility of representation.
in adaptivity of the whole system. This can test the hypotheses that the organizational complexity of biological networks is a source of its adaptability and survivability.

Figure 4 shows the hypergram for the face image data showing the performance profile for k-hypernetworks for \( k = 1, \ldots, 64 \). The training data for this problem contains 2630 examples and the test set contains 1130 examples of 64-bit image. It is interesting that the hypernetworks show a good performance in the low-k range, meaning there are useful modules in the low-dimensional subspace. The overall result suggests that microcircuits consisting of hyperedges of size \( k = 1 \) to 20 (or 30 for large network sizes) contain high information content for this specific data set. Note that the performance degrades for \( k > 20 \) (and \( k > 30 \) for large networks). This seems attributed to the fact that as \( k \) grows the probability of a test sample being matched to a training sample gets smaller.

For this problem, \( |X| = 64 \) and the size of the full search space is \( |E| = 2^{64} \). According to this simulation result, for \( k = 20 \), the \( k \)-hypernetwork consisting of \( |E(H^{(k)})| = 100,000 \) hyperedges (= 2,000,000/20) achieves a good performance. The effectivenss of this search can be expressed as the ratio \( r = \frac{|E(H^{(k)})|}{|E|} = \frac{100,000}{2^{64}} << 1 \). This suggests that, though the full search space is intractably big, the random hypernetwork manages to handle this problem. We have compared the performance of hypernetworks with the state-of-the-art machine learning models, such as multilayer perceptrons, naive Bayes classifiers, decision trees, \( k \)-nearest neighbors, and support vector machines, and obtained very competitive results. The best performance of 95.1 % was obtained by \( k \)-nearest neighbors with \( k = 3 \), and the hypernetworks obtained 94.4 % with uniform hyperedge size of 33. The hypernetworks outperformed all the other methods.

Figure 5 shows a similar trend for the face image data set. This task consists of 150 face images for training and 15 test images, each consisting of 480 bits (Yale face data). The hypernetworks generated by the random graph process biased by the training set achieved a competitive performance for the range of \( k = 20 \) to 50. The complete search space is of size \( 2^{480} \). For \( k \)-hypernetworks, the effective ratio of search for \( k = 30 \) is \( r = \frac{|E(H^{(k)})|}{|E|} = \frac{1,500,000}{2^{480}} << 1 \), where the number 1,500,000 comes from 10,000 hyperedges \times 150 images (of 15 people).

The effect of noise in sampling and performance was investigated. Biological cells seem robust against environmental noise and perturbations [9][12]. We test this effect in our surrogate data by randomly corrupting the digit images. Figure 6 shows the classification error \( (y\text{-axis}) \) vs. the corruption intensity \( (x\text{-axis}) \) for various \( k \) values. As expected, the error rate increases as the corruption intensity increases. The error increases more dramatically for large \( k \)-hypernetworks than for small \( k \)-hypernetworks. This implies...
that high $k$-hypernetworks are more susceptible to data corruption. Conversely, the low $k$-hyperedges are more robust to build a reliable system when faced with noisy environments. The diversity of the system components can be increased further by incorporating hyperedges of various $k$'s. Figure 7 shows the evolution of the hypergrams in the complete 10-hypernetwork. The data set came from microarray experiments. Ten genes were selected to build a hypernetwork classifier for disease diagnosis. The learning process started with a complete, but randomly instantiated hypernetwork and the hyperedges in the current network are amplified or retracted depending on their match with the hyperedges sampled from the training data. The training proceeded by repeatedly sweeping the training set to sample more hyperedges. Each sweep constitutes an epoch. The figure shows the general trend that, as learning proceeds, the frequency of small hyperedges tends to increase while that of large hyperedges tends to decrease. This seems to conform to the Occam’s razor principle, i.e. simple models should be preferred to complex models when everything else is the same [18]. This is especially interesting since the biased random graph process tends to reduce the complexity of the system even though we did not enforce any explicit complexity penalty. This seems because smaller hyperedges are less susceptible to the noise than the larger ones.

V. CONCLUSION

We introduced the random hypernetwork architecture inspired by biomolecular networks in cells. The network consists of a large number of heterogeneous “micromodules” (i.e. hyperedges) which interact with each other in a massive way to build potential “microcircuits”. We analyzed the structural properties of the hypernetworks to cope with a short-term change (adaptability) and a long-term change (Persistency) in the environment, where the environment was simulated by a sequence of training examples. For intelligent organisms, including humans, learning is a capability useful to cope with the first kind of perturbations, and memory is a faculty necessary to deal with the second kind of change.

Our analysis suggests that large micromodules are advantageous to agile learning of specific examples while small micromodules are useful to keep the hypernetwork system stable and persistent for a wide range of inputs in the longer term. This kind of specific yet stable behavior is also found in interaction and transcriptional regulatory networks in cells [9] and neuronal synapses [8][10]. This observation offers an important lesson for designing computational learning systems. Most of neural network architectures are designed to consist of high-dimensional, fine-tuned components of homogeneous structure, which is not necessarily the best strategy to build a computational intelligence system that prospers and survives across the entire life. Applied back to biology, it would be also interesting to see if the random hypernetworks identify motifs and modules of real biological networks.

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