Springer Nature 2021 LATEX template

# Biological Neurons Compete with Deep Reinforcement Learning in Sample Efficiency in a Simulated Gameworld

Moein Khajehnejad<sup>1,2†</sup>, Forough Habibollahi<sup>1†</sup>, Aswin Paul<sup>2,3</sup>, Alon Loeffler<sup>1</sup>, Adeel Razi<sup>2,4,5</sup> and Brett J. Kagan<sup>1\*</sup>
<sup>1</sup>Cortical Labs Pty Ltd, Melbourne, 3056, VIC, Australia.
<sup>2</sup>Turner Institute for Brain and Mental Health, Monash University, Clayton, 3800, VIC, Australia.
<sup>3</sup>IITB-Monash Research Academy, Mumbai, India.
<sup>4</sup>Wellcome Centre for Human Neuroimaging, University College London, WC1N 3AR, United Kingdom.
<sup>5</sup>CIFAR Azrieli Global Scholars Program, CIFAR, Toronto,

Canada.

\*Corresponding author(s). E-mail(s): brett@corticallabs.com; <sup>†</sup>The authors contributed equally to this work.

#### Abstract

How do biological systems and machine learning algorithms compare in the number of samples required to show significant improvements in completing a task? We compared the inherent intelligence of in vitro biological neural networks to the state-of-the-art deep reinforcement learning (RL) algorithms in a simplified simulation of the game 'Pong'. Using DishBrain, a system that embodies in vitro neural networks with in silico computation using a high-density multi-electrode array, we contrasted the learning rate and the performance of these biological systems against time-matched learning from three state of the art deep RL algorithms (i.e., DQN, A2C, and PPO) in the same game environment. This allowed a meaningful comparison between biological neural systems and deep RL. We find that when samples are limited to a real-world time course, even these very simple biological cultures outperformed deep RL algorithms across various game performance characteristics, implying a higher sample efficiency. Ultimately, even when tested across multiple types of information input to

assess the impact of higher dimensional data input, biological neurons showcased faster learning than all deep reinforcement learning agents.

**Keywords:** In Vitro, Neural Cultures, Deep Reinforcement Learning, Synthetic Biological Intelligence, Sample Efficiency, Electrophysiology, Biocomputing, Learning, Intelligence

# 1 Introduction

Both biological and machine intelligence systems demonstrate the ability to learn and achieve goals. Although the complexity of, and drivers behind, these tasks may differ, comparisons between these types of systems can yield valuable insights [1]. Even definitions of what traits artificial intelligence should demonstrate are heavily informed by traits observed in biological intelligence [2, 3]. Yet comparisons between biological and machine intelligence have been notoriously difficult, as the scale of connections in even simple biological organisms far exceeds that found in artificial neural networks or comparable Machine Learning (ML) algorithms [4, 5]. However, by taking a system-based approach, we aimed to compare data gathered from a biological neural network (BNN) using the recently validated *DishBrain* system [6] against time-matched learning from deep reinforcement learning (RL) algorithms - DQN, A2C and PPO. Despite the inherent differences between silicon and biological systems - such as power consumption and network size - this approach makes it possible to explore learning performance and efficiency in these different systems to understand key differences in their information processing dynamics.

RL has become increasingly popular in the fields of ML and artificial intelligence by offering a way of programming agents through reward and punishment cues without having to specify how the task is to be accomplished. However, to deliver on this promise, formidable computational obstacles must be overcome. RL implies learning the best policy to maximize an expected cumulative long-term reward throughout many steps in order to achieve objectives (goals) [7]. A deep RL approach integrates artificial neural networks with an RL framework that helps the system to achieve its goals [8]. It maps states and actions to the rewards they bring, combining function approximation and target optimization. Reinforcement algorithms that incorporate deep neural networks have been developed to beat human experts in multiple game settings including: poker [9], multiplayer contests [10], complex board games, including go and chess [11–13] and numerous Atari video games [14]. Nevertheless, RL still faces real challenges including but not limited to: complexities in the selection of hyper-parameters and reward structure, sample inefficiency [15, 16], reproducibility issues [17], and catastrophic forgetfulness [18, 19]. Furthermore, to allow RL algorithms to train quickly requires considerable levels of computing power [20] with notable associated environmental impacts [21]. Finally, RL algorithms are typically trained for narrow tasks in static environments; where training and performance phases are separate [1, 19].

Holistically, these traits suggest that although deep RL algorithms are highly functional, their learning mechanisms almost certainly differ fundamentally from biological learning [1, 16, 22]. It is noted that RL as a mechanism has been found to elicit rapid and adaptable learning in animals [23, 24]. Yet it seems unlikely that similar underlying statistical mechanisms that support RL, such as back-propagation and gradient descent, have biological parallels in the brain [22, 25]. Ultimately, these mechanisms are likely too inefficient to be accepted as plausible models of human learning [15, 26, 27]. This is especially true when considering how intelligence may arise from cells without established pathways of motivation. Early work investigating how cells respond to stimulation that can be modified through their own activity showed rapid adaptation displayed through synaptic plasticity [28-30]. Furthermore, it was recently demonstrated that by using electrophysiological stimulation and recording in a real-time closed-loop system with a monolayer of living biological neurons, biological neural cells could be trained to significantly improve performance in a simulated 'pong' game-world [6]. The question arises as to whether the observed performance in these simple BNNs is notable compared to that of RL at the same task, especially regarding sample efficiency.

*DishBrain* is a novel system shown to display simple biological intelligence by harnessing inherent adaptive properties of neurons. In DishBrain, in vitro neuronal networks are integrated with *in silico* computing via high-density multi-electrode arrays (HD-MEAs). These cultured neuronal networks showcase biologically-based adaptive intelligence within a simulated gameplay environment in real-time through closed-loop stimulation and recordings [6]. Specifically, BNNs exhibited self-organised adaptive electrophysiological activity that was consistent with an innate ability to learn and showcase an intelligent response to limited - although biologically plausible [31] - structured external information. Data was generated from cortical cells obtained from either embryonic rodent or human induced pluripotent stem cell (hiPSC) sources. These cell types were compared to assess reproducibility of learning effects across species and preparations. Here, we investigate whether these elementary learning systems achieve performance levels that can compete with state-of-the-art deep RL algorithms. Additionally, by varying the input information density presented during training of the RL algorithms, we can determine the impact of information sparsity and ensure suitable comparisons to the biological system. This is the first comparison between a Synthetic Biological Intelligence (SBI) system [32] and state-of-the-art RL algorithms. This research aims to investigate whether simple biological systems can demonstrate characteristics compared to established RL methods to justify further research in this area, either where SBI systems are standalone learning devices, or inform further algorithm development in the ML space. We anticipate that SBI systems will exhibit greater sample efficiency than RL models, as suggested by prior research. However, this entails constraining training

to a real-time approximate sample count for RL algorithms. Moreover, this work explores biological reorganisation in the biological *DishBrain* system facilitating the observed learning.

Figure 1.a,b illustrate the input information, feedback loop setup, and electrode configurations in the *DishBrain* system and Figure 1.c illustrates the comparison between input information in the *DishBrain* system and deep RL algorithms.



Fig. 1 DishBrain system and Various input designs to RL algorithms. a) DishBrain feedback loop setup and Electrode configuration and predefined sensory and motor regions. Figures adapted and modified from [6]. b) Schematic comparing the information input routes in the DishBrain system (left) and the three implementations of the deep RL algorithms (right). In each design, the input information to the computing module (deep RL algorithms or DishBrain) is denoted by a vector I.

# 2 Results

Game performance of human cortical cells (HCCs; 174 sessions) and mouse cortical cells (MCCs; 110 sessions) was compared with three RL baseline methods. To determine how learning arises both in cultures and in baseline methods, three key gameplay characteristics were examined. These include: mean hit-to-miss ratio (average hits-per-rally), number of times the paddle failed to intercept the ball on the initial serve (aces), and number of long rallies or episodes ( $\geq 3$  consecutive hits).

For comparison, every 70-episode run of each RL algorithm was mapped to approximately 20 real-time minutes by normalizing the actual total length of each run in minutes and then multiplying by 20. This approximates the number of rallies biological cultures would experience in a 20-minute session. Details of the implemented RL algorithms and information about the selected hyper-parameters are included in Supplementary Materials A.4. Figures 2, 3, and 4 represent the main findings for comparisons between biological cultures and the IMAGE INPUT, PADDLE&BALL POSITION INPUT, and BALL POSITION INPUT designs of the RL methods. The intent behind different input designs was to determine whether varying the amount of information input into the algorithm altered sample efficiency and learning characteristics of these systems. In particular, the PADDLE&BALL POSITION INPUT, and BALL POSITION INPUT methods were intended to be more accurate comparisons to the information density presented to the DishBrain system. Extended Data Tables S3 and S4 present all multivariate statistical tests performed in relation to the following results. All *post-hoc* follow-up tests are presented in Extended Data Table S2.

### 2.1 Comparison in performance between *DishBrain* and three RL algorithms with various information densities

In all three designs, biological cultures (i.e. HCC and MCC) outperform all RL baseline algorithms (see Subfigures 2.a, 3.a, and 4.a) in terms of the highest level of average hits-per-rally achieved. The cultures demonstrate faster learning rates over time. Subfigures 2.b, 3.b, and 4.b compare the % of aces among the biological cultures and the RL groups given the three different designs. HCC and MCC achieve the lowest percentage of aces compared to the deep RL algorithms in Subfigure 2.b and the other RL baseline designs in Subfigures 3.b, and 4.b. The increasing trend in % of long rallies is observed in all groups and among all designs except the DQN and PPO groups in the IMAGE INPUT design and PPO in the PADDLE&BALL POSITION INPUT design, as illustrated in Subfigures 2.c, 3.c, and 4.c. Average % of long rallies was highest for MCC and HCC compared to RL baselines.

Key activity metrics in the first 5 minutes versus the last 15 minutes in each session were compared to identify any significant improvement occurring in the learning process within each group.



Image Input to the deep RL algorithms. a) Schematic highlighting figure Fig. 2 comparisons are between biological DishBrain system and an pixel-based information input to te RL algorithms. Average number of **b**) hits-per-rally, **c**) % of aces, and **d**) % of long rallies over 20 minutes real-time equivalent of training DQN, A2C, PPO, and MCC, HCC cultures. A regressor line on the mean values with a 95% confidence interval highlights the learning trends. Comparing the performance amongst all groups, the highest level of average hits-per-rally is achieved by the neuronal MCC and HCC cultures while PPO is outperformed by all the opponents. The average % of aces is lowest for the neuronal cultures compared to all deep RL baseline methods. The average % of long rallies reaches its highest levels for MCC and HCC. e) Average performance of groups over time. Only biological cultures have significant within-group improvement and increase in their performance at the second time interval (One-way ANOVA test, p = 5.854e-6, p = 7.936e-17, for MCC and HCC respectively; p = 0.231, p = 0.318, and p = 0.400 for DQN, A2C, and PPO respectively). f) Average % of aces within groups and over time. Only MCC and HCC (One-way ANOVA test, p = 0.014, p = 2.907e-08, respectively) differed significantly over time. No significant change was detected within the DQN, A2C, or PPO groups (One-way ANOVA test, p =0.080, p = 0.195, and p = 0.308, respectively). g) Average % of long-rallies ( $\geq 3$ ) performed in a session. All groups showed an increase in the average number of long rallies where this within-group increase was significant only for MCC, HCC, and A2C (One-way ANOVA test, p = 1.172e-7, p = 1.525e-24 for MCC and HCC, respectively and p = 0.605, p = 0.002, and p = 0.684 for DQN, A2C, and PPO, respectively). \*p < 0.05, \*\*p < 0.01, and \*\*\*p < 0.001. h) Pairwise Tukey's post-hoc test shows that HCC and MCC groups significantly outperform PPO, A2C, and DQN in the last 15 minutes interval. i) Using pairwise Tukey's post-hoc test, the HCC group significantly outperforms the PPO in the last 15 minutes interval with a lower average of % Aces. A2C also outperforms PPO in this time interval. j) Pairwise comparison using Tukey's test only shows a significant difference in the percentage of long rallies between HCC and the rest of the groups in the first 5 minutes. However, this is later altered in the direction of all groups having an increased % of long rallies with MCC outperforming PPO in the last 15 minutes of the game. Box plots show interquartile range, with bars demonstrating 1.5X interquartile range, the line marks the median and the black triangle marks the mean. Error bands = 1 SE

Panel (d) in Figures 2, 3, and 4 compares average rally length between the two defined time intervals within groups. The results imply that the withingroup increasing trend in rally length is significant only in the biological groups.

Panel (e) in Figures 2, 3, and 4 represents the change in average percentage of aces over time. A significant decrease in number of aces (where the ball was missed immediately in an episode with no accurate hits) implies an improved game performance. Only MCC and HCC had a significant decrease in average ace percentage as opposed to the rest of RL based algorithms with different input designs.

Panel (f) in Figures 2, 3, and 4, shows that the percentage of long rallies in the first 5 minutes versus the last 15 minutes only significantly increased for biological cultures and A2C with the IMAGE INPUT and BALL POSITION INPUT designs.

Inter-group comparison was carried out for both time intervals (0-5 and 6-20 minutes) and all three metrics using Tukey's post-hoc test as represented in panels (g), (h), and (i) in Figures 2, 3, and 4 for rally length (i.e. hit counts), % of aces, and % of long rallies respectively.

Note, in the IMAGE INPUT design, where average rally length of deep RL methods comes closest to the biological cultures, the input information density is starkly different between the two groups. While RL agents received pixel data with a density of  $40 \times 40$  pixels, biological cultures only receive input from 8 stimulation points with a given integer rate code of 4Hz–40Hz, high-lighting important efficiency differences in informational input between these learning systems. The possibility of higher input information dimensionality having adverse effects on overall sample efficiency of RL algorithms is further nullified by evaluating two alternative input structures (PADDLE&BALL POSITION INPUT and BALL POSITION INPUT designs).

### 2.2 Examining impact of paddle movement speed on learning rates

To account for potential effects of paddle movement speed and whether it plays an important role in determining the success rate of paddle control, we derived the average paddle movement (in pixels) for all groups. Subfigures 5.a,c, and e represent these results for the IMAGE INPUT, PADDLE&BALL POSITION INPUT, and BALL POSITION INPUT designs, respectively. Using Tukey's posthoc tests, a consistently significant difference between pairs of DQN, PPO or A2C with MCC or HCC was found in terms of average paddle movement, with RL algorithms having the higher average. This occurs when all the RL algorithms with different input designs have significantly higher average paddle movement compared to both groups of biological cultures. As per previous findings [6], increased paddle movement speed in RL algorithms does not translate to improved game performance, likely suggesting a more stochastic paddle control.





Fig. 3 Paddle&Ball Position Input to the deep RL algorithms. a) Schematic highlighting figure comparisons are between biological DishBrain system and paddle and ball position information input to RL algorithms. Average number of b) hits-per-rally, c) % of aces, and d) % of long rallies over 20 minutes real-time equivalent of training DQN, A2C, PPO, and MCC, HCC cultures. A regressor line on the mean values with a 95% confidence interval highlights the learning trends. The highest level of average hits-per-rally is achieved by the neuronal MCC and HCC cultures. The average % of aces is lowest for the neuronal cultures compared to all deep RL baseline methods. The average % of long rallies reaches its highest levels for MCC and HCC. Comparing to the same findings for the HCC and MCC groups, e) average rally length over time only showed a significant increase in the biological cultures between the two time intervals (One-way ANOVA test, p = 0.913, p = 0.958, and p = 0.610 for DQN, A2C, and PPO respectively). f) Average % of aces within groups and over time only showed a significant difference in the MCC and HCC groups. No significant change was detected within the DQN, A2C, or PPO groups (One-way ANOVA test, p =0.463, p = 0.338, and p = 0.544 respectively). g) Average % of long-rallies ( $\geq 3$ ) performed in a session increased in the second time interval in all groups. This within-group difference was only significant for the MCC and HCC groups (One-way ANOVA test, p = 1.172e-7, p = 1.525e-24, p = 0.233, p = 0.320, and p = 0.650 for MCC, HCC, DQN, A2C, and PPO, respectively). \*p < 0.05, \*\*p < 0.01, and \*\*\*p < 0.001. h) Pairwise Tukey's post-hoc test shows that the HCC group is significantly outperformed by A2C and PPO in the first 5 minutes in terms of the hit counts or rally length. Biological cultures, however, do significantly better compared to all deep RL opponents in the 15 minutes interval. i) Using pairwise Tukey's post-hoc test, HCC group significantly outperforms the DQN and A2C groups in the last 15 minutes interval with a lower average of % Aces. DQN is also outperformed by the MCC group in this time interval. j) Pairwise comparison using Tukey's test shows a significant difference in the percentage of long rallies between HCC and the rest of the groups in the first 5 minutes all outperforming the HCC. However, this is later altered in the last 15 minutes with only MCC outperforming PPO significantly having an increased % of long rallies. Box plots show interquartile range, with bars demonstrating 1.5X interquartile range, the line marks the median, and the black triangle marks the mean. Error bands = 1 SE



Fig. 4 Ball Position Input to the deep RL algorithms. a) Schematic highlighting figure comparisons are between biological DishBrain system and a ball position information input to RL algorithms. Average number of b) hits-per-rally, c) % of aces, and d) % of long rallies over 20 minutes real-time equivalent of training DQN, A2C, PPO, and MCC, HCC cultures. A regressor line on the mean values with a 95% confidence interval highlights the learning trends. The highest level of average hits-per-rally is achieved by the neuronal MCC and HCC cultures. The average % of aces is lowest for the neuronal cultures compared to all deep RL baseline methods. The average % of long rallies reaches its highest levels for MCC and HCC. Comparing to the same findings for the HCC and MCC groups, e) average rally length over time only showed a significant increase in the biological cultures between the two time intervals (One-way ANOVA test, p = 0.995, p = 0.812, and p = 0.547for DQN, A2C, and PPO respectively). f) Average % of aces within groups and over time only showed a significant difference in the MCC and HCC groups. No significant change was detected within the DQN, A2C, or PPO groups (One-way ANOVA test, p = 0.241, p = 0.581, and p = 0.216 respectively). g) Average % of long-rallies ( $\geq$  3) performed in a session increased in the second time interval in all groups except DQN. This within-group difference was only significant for MCC, HCC, and A2C groups with p = 0.002 for the A2C group. \*p < 0.05, \*\*p < 0.01, and \*\*\*p < 0.001. h) Pairwise Tukey's post-hoc test shows that biological cultures significantly outperform all deep RL groups in the last 15 minutes in terms of the hit counts or rally length. i) Using pairwise Tukey's post-hoc test, the HCC group significantly outperforms all the deep RL groups in the last 15 minutes interval while MCC also outperforms DQN with a lower average of % Aces. j) Pairwise comparison using Tukey's test shows a significant out-performance of all groups over HCC in the percentage of long rallies in the first 5 minutes. In the second time interval, MCC shows a significantly higher % of long rallies compared to DQN with HCC now being outperformed only by A2C. Box plots show interquartile range, with bars demonstrating 1.5X interquartile range, the line marks the median and the black triangle marks the mean. Error bands = 1 SE

Subfigures 5.b, d, and f compare relative improvement in performance between biological cultures and RL algorithms for IMAGE INPUT, PAD-DLE&BALL POSITION INPUT, and BALL POSITION INPUT, respectively. This measure identifies the relative increase in average accurate hit counts in the second 15 minutes of the game compared to the first 5 minutes. The HCC group shows the highest improvement in time. Post-hoc tests showed significant differences between HCC and all the RL methods across all of the three different input designs. The MCC group also outperforms PPO in both IMAGE INPUT and PADDLE&BALL POSITION INPUT designs as well as DQN and A2C in the IMAGE INPUT and PADDLE&BALL POSITION INPUT designs, respectively.

Subfigures 5.g, h, i, and j compare frequency tables for distributions of mean summed hits per minute amongst groups for the IMAGE INPUT, PAD-DLE&BALL POSITION INPUT, and BALL POSITION INPUT designs respectively. These tables were not significantly different (Two-sample *t*-test).

Details of the implemented algorithms and hyper-parameters can be found in the data repository provided in Section 4.5. For further exploration of selected hyper-parameters, see Supplementary Materials A.5, A.4 and Extended Data Figures B2, B3, B4, B5, B6, B8, and B9. In summary, it was found that similar results were obtained across a variety of hyper-parameters, strongly supporting the initial conclusions of this work.

### 2.3 Exploring biological neural networks activity reorganization within learning sessions

The apparent highly sample efficient learning of BNNs remained starkly different from the RL algorithms. This sparked the mechanistic question as to whether this performance difference was accompanied by an equally distinct and rapid system-wide reorganization of neural activity while cells were embodied in a *Gameplay* environment, versus displaying spontaneous activity during rest. To explore this question, we analyzed spiking activity of each HD-MEA channel to assess neuronal network dynamics and functional connectivity. Understanding these complex dynamics is crucial for uncovering the neural mechanisms behind the efficient learning that occurs in BNNs. We characterized complex network dynamics in *in-vitro* neuronal systems during two distinct activity states: spontaneous activity state with no stimulation (*Rest*) and engagement in the previously discussed game environment of *pong* (*Gameplay*).

A network matrix using functional connectivity – defined as pairwise zerolag Pearson correlations – among all channels was constructed for the entire duration of all recordings. Figure 6.a - i. represent changes in network functional connectivity when comparing the full duration of *Gameplay* and *Rest* recordings from all of the 1024 channels available on the HD-MEA. Using oneway t-tests, significant differences between *Gameplay* and *Rest* were found for the number of nodes, number of edges, density, mean participation coefficient (pcoeff), average weight, and modularity index. No significant differences



Biological Neurons vs Deep Reinforcement Learning

Fig. 5 Paddle movement and relative improvement. The average paddle movement in pixels in all the different groups for the a) IMAGE INPUT, c) PADDLE&BALL POSITION INPUT, and e) BALL POSITION INPUT to the deep RL algorithms. Tukey's post-hoc test was conducted showing that DQN, PPO, and A2C had a significantly higher average paddle movement compared to HCC and MCC in all scenarios. Relative improvement (%) in the average hit counts between the first 5 minutes and the last 15 minutes of all sessions in each separate group for the b) IMAGE INPUT, d) PADDLE&BALL POSITION INPUT, and f) BALL POSITION INPUT to the deep RL algorithms. The biological groups show higher improvements with HCC outperforming all. b) Using Games Howell post-hoc test, the inter-group differences were significant with HCC outperforming all other groups, as well as MCC significantly outperforming PPO. d) HCC showed a significantly higher relative improvement compared to all the other groups while MCC also outperformed A2C and PPO in terms of relative improvement over time. f) Finally, HCC could still perform significantly better than all the deep RL groups with the BALL POSITION INPUT design to the deep RL algorithms with MCC outperforming PPO and DQN in this design. Distribution of frequency of mean summed hits per minute amongst groups for g) biological cultures and deep RL algorithms with h) IMAGE INPUT, i) PADDLE&BALL POSITION INPUT, and j) BALL POSITION INPUT.

were found for clustering coefficient, max betweenness, and characteristic path length.

Recently, there has been a notable emphasis on extracting insights from complex and high-dimensional networks by obtaining network embeddings in lower dimensions [34-36]. Motivated by this, we implemented a dimensionality reduction using the t-SNE algorithm [38] after dividing recording sessions in half. Results presented in Figure 6.j, showcase t-SNE outcomes with colorcoded distinctions for the initial and latter portions of 20-minute *Gameplay* and 10-minute *Rest* sessions across three samples. Discernible patterns emerge in *Gameplay* but not in *Rest*, signifying distinctive network dynamics during the learning process, predominantly observed in *Gameplay* which was effectively captured in this lower dimensional space.

Furthermore, in light of previous findings that in complex neural networks only a subset of neurons becomes active at any given moment and many do not exhibit distinct action potentials [39], our objective was to enhance the

reduction of computational complexity when studying these neuronal populations while maintaining the dynamic properties of the network. Utilizing the method introduced in [37], we identified a subset of key neurons (30 neurons) characterizing the network's behavior during *Gameplay*, to more efficiently study this smaller and more interpretable network.

Next, by utilizing these low-dimensional representations, we recreated functional connectivity matrices from these 30 channels as nodes, and edges represented by Pearson correlations as described previously.

After constructing the connectivity networks, we aimed to examine their temporal evolution in both *Gameplay* and *Rest*. To achieve this, we divided each recording session into 2-minute windows and evaluated the change in edge weights as the network evolved over those windows.

Figure 6.k. shows differences in the correlation between each pair of nodes when comparing the last and first 2 minutes of each recording. This figure shows the average networks over all *Gameplay* or *Rest* sessions with red/black colors indicating increased/decreased correlations, respectively. The edge weights are proportional to the absolute value of these differences in functional connectivity. Details of the utilized pipeline to construct these connectivity networks are outlined in 4.3, and Supplementary Materials A.6 and Extended Data Figure B10.

We found that biological cultures, while embedded in the game environment, had a higher number of edges with increased correlation between channels. This change was not apparent during rest state spontaneous activity. This indicates significant network plasticity in these cultures that can be a necessary underlying mechanism for the learning that happens in this closed-loop system [6]. Moreover, we evaluated the network characteristics from all generated networks and compared them between the first and last 2 minutes of recordings in both *Rest* and *Gameplay* groups. Figures 6.1 - p. show these results. All of these metrics except characteristic path length showed statistically significant differences during *Gameplay*, but not in *Rest*. Particularly, the average weight of the networks only shows a significant increase in the *Gameplay* sessions and modularity index significantly decreases only during *Gameplay*. A higher modularity index indicates the presence of many connections within a community but only few with other communities, while a lower index means higher outward connections between different communities.

# 3 Discussion

The advantages and disadvantages of biological versus machine intelligence are often discussed, yet technical limitations have prevented meaningful comparisons in terms of performance. In this work, we compare performance of biological neuronal networks with that of state-of-the-art deep reinforcement algorithms (deep RL). Using a controllable game environment of a simplified *pong* simulation, it was possible to compare key traits between these different



Fig. 6 Significant network plasticity occurs in biological cultures when embodied in the game environment. a - i) Network summary statistics of 1024 recorded channels using the full duration of all *Gameplay* and *Rest* sessions. Using one-way t-tests, we found significant differences in the number of nodes (p = 3.072e-03), number of edges (p =8.396e-26, density (p = 1.009e-25), mean participation coefficient (pcoeff) (p = 3.400e-02), average weight (p = 8.910e-20), and modularity index (p = 4.129e-13) between Gameplay and Rest. No significant differences were found for clustering coefficient (p = 0.568), max betweenness (p = 0.890), or characteristic path length (p = 0.533). j) Low-dimensional representation of 3 samples of *Gameplay* and their following *Rest* sessions using t-SNE. Purple and maroon dots are channel representations in the embedding space in the first and second half of the recordings. k) The average connectivity networks using the 30 representative channels over all the *Gameplay* and *Rest* sessions with edge weights representing changes in functional connectivity between channel pairs when comparing the last 2 minutes to the first 2 minutes of recordings. Edge colors signify the direction of these connectivity changes, with red indicating increases and black indicating decreases. Motor and sensory region channels are represented by blue squares and green circles, respectively. Arrows on motor region nodes show the paddle's movement direction as per their position in the predefined layout in Figure 1.b. 1 - p) Network summary statistics between the first and last 2 minutes of Gameplay and Rest recordings using the 30 representative channels in the lower-dimensional space. All of these metrics except the characteristic path length showed statistically significant differences using one-way ANOVA during Gameplay (p = 2.265e-3, p = 8.478e-8, p =1.891e-6, p = 1.005e-4, and p = 0.071, respectively), but not in the *Rest* condition of the cultures (p = 0.864, p = 0.670, p = 0.738, p = 0.281, and p = 0.899, respectively). \*p < 0.05, \*\*p < 0.01, and \*\*\*p < 0.001.

learning systems, with a focus on sample efficiency. Human or mouse cortical cells (HCC or MCC) along with three deep RL algorithms (DQN, A2C, and PPO), were compared in sessions with an average episode number of 70 games played. While direct comparisons between these systems are naturally constrained (even what is referred to as a "neuron" is inconsistent between fields of research), the aim of this work was to determine whether meaningful performance differences would arise between learning systems that may merit further exploration of BNNs as information processing machines. This approach allowed an examination of the overall performance of each group with respect to various gameplay characteristics and, for the RL methods, in response to varying information input.

Across all types of information input, BNN outperformed all RL baselines in terms of average hit-per-rally (Subfigure 2.a), % of aces (Subfigure 2.b), and % of long rallies achieved (Subfigure 2.c). Moreover, the increase in average rally length, decrease in number of aces, and increase in number of long rallies were significant only within the HCC and MCC groups and the A2C algorithm with the IMAGE INPUT and BALL POSITION INPUT designs in terms of the increase in the percentage of long rallies, when comparing the first 5 and the last 15 minutes during gameplay (see Subfigures 2.d, e, and f). Additionally, we found that the HCC group had the highest relative improvement in average number of hits between the first 5 minutes and last 15 minutes of the game as depicted in Subfigures 5.b, d, and f.

Results show that the game performance of deep RL algorithms in terms of relative learning improvement in time and average hits-per-rally is outperformed by biological cultures when number of allowable samples are fixed. This supports the conclusion that RL algorithms showed significantly lower sample efficiency compared to BNN, having lower improvements in learning over an episode-matched training duration provided for all groups. This matches theoretical expectations previously outlined where it was proposed that biological learning is inherently more sample efficient [1, 22]. Given how rapidly synaptic plasticity or behaviour changes have occurred for both in vitro and in vivo models, this finding is consistent with such observations [23, 24, 28, 29, 41]. Here we extend upon previous work by examining the functional connectivity of BNNs and observing both rapid and robust changes across multiple metrics during gameplay, compared to when unstimulated (rest). Furthermore, although difficult to directly compare energy consumption, it should be noted that biological systems use magnitudes less than traditional computing systems used for ML [42].

Moreover, the comparison between the various machine learning algorithms is also consistent with past research. A2C and PPO often achieve better results compared to DQN which is in line with previous studies proposing that algorithms optimizing a stochastic policy generally perform better than DQN [? ?] which is known to suffer more from low sample efficiency [52]. This can best be seen in the relative performance between different levels of information input. When a CNN was integrated into the RL models, some degree of learning (that did not reach statistical significance) was observed for these systems. BNN received only a fraction of the input information density compared to their RL opponents in this condition (8-pixel combination of rate coded and place coded stimulation compared to  $40 \times 40$  pixels of the input image). Moreover, it was reasonable to consider whether the curse of dimensionality (where higher dimension input can require additional episodes to converge to a minima) may be adversely impacting the RL agents under the IMAGE INPUT condition. To account for potential disadvantages occurring as a result of increased input dimensionality, we also examined two alternative designs for input structure to the RL algorithms (i.e. PADDLE&BALL POSITION INPUT and BALL POSITION INPUT designs). In-depth comparison between BNN performance and these alternative RL algorithms did not provide any significantly different outcome in favour of the RL baselines' sample efficiency (see Figures 3 and 4).

That BNN could perform with such sparsely coded informational input conforms to coding mechanisms known to be used in biological intelligence [31, 43, 44]. While RL algorithms use back-propagation, it has been argued that this method is likely too inefficient to function within biological systems [15, 22, 25–27, 45]. A more dynamic reconfiguration of network activity has been proposed to be necessary for the learning rates observed in biological cultures [15, 26, 27, 46]. Theories of how this learning may occur include predictive coding, active inference, prospective configurations, and Hopfield networks, which have been used to describe how neural systems may reorganise activity for learning tasks [26, 47–50]. While nuances amongst these different theories exist, the general notion supports the idea of a more biological consistent forward-based learning process compared to backpropagation.

To explore this, we explored a biologically inspired algorithm, implementing an active inference agent that uses counterfactual learning and reported the comparison results in Supplementary Materials A.7 and Extended Data Figure B11. Improved learning rates observed in the biological inspired learning protocol supports the potential of active inference agents to provide valuable insights into optimized learning strategies, thereby enhancing our understanding of these dynamics. However, these active inference algorithms are still highly dependent on the chosen hyper-parameters and require relatively higher power consumption compared to biological systems. Nonetheless, these results highlight the value of further exploring biologically-inspired systems of learning and support the notion that SBI systems may offer a useful pathway to do this in the future. Considering that biological neural systems can also work massively in parallel, it is likely that learning effects observed in this work also relate to observed network-wide alterations in activity, which have been difficult to implement algorithmically as they are not yet fully understood [6, 41]. Our analyses of functional connectivity network dynamics observed in the biological cultures during gameplay versus rest reveals the scope and speed with which these systems can reorganize activity. These results support the value of investigating dynamic algorithms which allow network reorganization in response to changing environments to improve sample efficiency in future

ML algorithms. Interplay between individual neuronal activity and population level activity adds further complexity to determining the mechanisms of learning within biological cultures. While limitations in study design (specifically the use of opaque chips) prevent a robust assessment of the specific learning processes within the cultures used in this study beyond that previously reported [6, 41], findings endorse this approach for future exploration of these dynamics with altered study designs. Future work has potential to not only understand how biological intelligence arises, but also how one may implement more advanced biologically inspired learning protocols that may surpass current performance.

This work acts as the first direct comparison (to our knowledge) between an SBI system and state-of-the-art RL algorithms on a comparable task. A potential limitation of the work results from the fact that the space of hyperparameters is too large for an exhaustive search in each algorithm. However to explore a significant number of hyper-parameters we used values utilized in the original paper that introduced each algorithm. We tuned the hyperparameters that were most sensitive by a grid search in a limited space of those parameters. As a result of their sensitivity to hyper-parameter selection, state-of-the-art deep RL algorithms remain challenging to apply. The use of model-based RL is proposed for achieving higher sample efficiencies. Model-free algorithms, however, often perform significantly better asymptotically than these algorithms [51]. Recently, different accelerated approaches have also been proposed for deep RL [51-53]. Nonetheless, many still lag behind the performance of the original algorithms or require modern computers and a combination of CPUs and GPUs prompting even higher computational costs [54]. As a future pathway, these modified algorithms may be utilized for further comparisons. Arguably, biological cultures operating with the DishBrain system do not require such fine-tuning of parameters or manipulation of the architecture.

Nonetheless, the results of this work supports that even rudimentary SBI systems with limited informational input are viable learning systems that can compete and even outperform established RL algorithms on sample efficiency. Coupled with the promise of significant gains in power efficiencies, flexibility of tasks, and upcoming improvements in the associated technologies[55], these biological-based intelligence systems present a compelling pathway for realizing real-time learning unachievable by current silicon-based approaches alone.

# 4 Methods

### 4.1 DishBrain System

The initial validation of the *DishBrain* system was previously presented in [6]. Briefly, cortical cells were either differentiated from human induced pluripotent stem cells (hiPSC) using a modified Dual SMAD inhibition protocol or surgically extracted from E15 mouse embryos. By setting up cultures from multiple cell sources this helped ensure that results would generalize across different species and preparations. Ethical approvals for animal work were obtained (E/1876/2019/M: Alfred Research Alliance Animal Ethics Committee B) for animal work with all cell culture work according to relevant ethical guidelines. Cell line characterisation and approvals are reported in [6].

Approximately  $10^6$  cells were plated and integrated onto a high-density multi-electrode array (HD-MEA; Maxwell Biosystems, AG, Switzerland). Cell cultures were maintained in BrainPhys<sup>™</sup> Neuronal Medium (Stemcell Technologies Australia, Melbourne, Australia) supplemented with 1% penicillinstreptomycin during testing. The DishBrain system was developed as a low latency, real-time system which interacts with the HD-MEA software to allow closed-loop stimulation and recording which has previously been described in detail [6]. Using this method, activity from a neuronal culture can be read, along with providing structured stimulation to the same culture in real-time. DishBrain was then utilized to embody neural cultures in a virtual game-world, to simulate the classic arcade game 'Pong'. Biphasic electrical stimulation was used to stimulate neurons consistent with previous attempts to elicit action potentials in comparable cultures [56]. Electrical stimulation was arranged to transmit a variety of task-related information between the cells and the simulated virtual environment using appropriate coding schemes via routed electrodes on the MEA that were divided into discrete regions as in Figure 1.b.

Specifically, stimulation was applied using a combination of rate coding (4Hz - 40Hz) electrical pulses to communicate the position on the x-axis and place coding (on a given electrode that was arranged topographically from an egocentric representation for the culture) to communicate information on the y-axis into a predefined bounded two-dimensional sensory area consisting of 8 sensory electrodes to deliver this input information. Three types of input were provided: the sensory stimulation as explained above, or stimulation in response to activity designated as either 'Predictable' or 'Unpredictable' feedback (see Figure 1.a). Cultures received Unpredictable stimulation when they missed connecting the paddle with the 'ball', i.e. when a 'miss' occurred. Using a feedback stimulus at a voltage of 150 mV and a frequency of 5 Hz, an unpredictable external stimulus could be added to the system. Random stimulation took place at random sites over the 8 predefined sensory electrodes at random timescales for a period of four seconds, followed by a configurable rest period of four seconds where stimulation paused, then the next rally began. Should no miss occur, the game would continue until either a miss occurred or the timer of 20 minutes expired, which would end the session. In contrast, cultures were exposed to Predictable stimulation when a 'hit' was registered - that is, when the 'paddle' connected successfully with the 'ball'. This was delivered across all 8 stimulation electrodes simultaneously at 75mV at 100Hz over 100ms and replaced other sensory information for 100 ms.

The movement of the paddle was controlled by the level of electrophysiological activity measured in a predefined 'motor area' of the cultured network as shown in Figure 1.b., which was collected in real-time. Incoming samples were filtered with a 2nd order high-pass Bessel filter with 100Hz cut-off. The

absolute value was smoothed using a 1st order low-pass Bessel filter with a 1 Hz cut-off and the spike threshold is proportional to this smoothed absolute value. A relative activity spike of 6 sigma greater than background noise was then used to define an action potential. Detected action potentials from counterbalanced motor regions were then summed together, where higher activity in a given pair of regions would cause the virtual paddle to move in one direction, while activity in the other regions would result in the inverse movement. Information about ball position relative to the paddle was adjusted in a closed-loop manner with a spike-to-stim latency of approximately 5ms. Figure 1.a,b illustrate the input information, feedback loop setup, and electrode configurations in the *DishBrain* system.

The gameplay performance of cell cultures subjected to the simplified pong environment via the *DishBrain* system was assessed. In each episode of the game, the average number of rallies before the ball was missed for the first time was then compared with different deep RL baseline methods. Each recording session of the cultures during gameplay was 20 minutes. During a gameplay session, the average number of rallies (i.e., episodes) an average biological culture would perform was  $69.04 \pm 7.95$  rallies/episodes. Therefore, to compare sample efficiency in a matched comparison, a total of 70 training episodes were provided to deep reinforcement learning algorithms during training.

More details of this system are introduced in Supplementary Materials A.1, A.2, and A.3 as well as Extended Data Figure B1.

### 4.2 Deep Reinforcement Learning Algorithms

In this work, we use three state-of-the-art deep reinforcement learning algorithms: Deep Q Network (DQN) [14], Advantage Actor-Critic (A2C) [57] and Proximal Policy Optimization (PPO) [58], established to have good performance in Atari games. Benefiting from deep learning advantages in automated feature extraction, specifically exploiting Convolutional Neural Networks (CNN) in their structures, these methods are robust tools in reinforcement tasks, particularly in games where the system's input is an image. In this work, aiming to account for potential detriments to sample efficiency resulting from the increased dimensionality of the image input to the deep RL algorithms [59], we designed two additional types of input information to the RL algorithms. We compare all three different designs with the performance of biological cultures. We attempt to study whether the curse of dimensionality and increased size of the feature vectors when directly utilizing image inputs affect the comparison between biological cultures and RL algorithms in terms of their sample efficiency. All the algorithms follow a common strategy although they are different in structure. The three different input categories and RL algorithm designs are introduced below:

• Image Input: The current state is a tensor of the difference of pixel values from the two most recent frames (i.e. another 40 × 40 grayscale pixel image)

<sup>1</sup>. This current state is then input into the CNN to obtain the selected action. Next, based on the action taken, a reward is received, and a new state is formed. The ultimate goal is to find a policy that indicates the best action in each state to maximize the reward function.

- Paddle&Ball Position Input: Instead of the gravscale image, a 4dimensional vector encoding the x and y coordinates of the ball (distance to the paddle/wall and distance to the floor in pixels) and the y coordinates of the paddle's top and the bottom was obtained. All values are integers between [4, 40]. The current state which is the input to each algorithm is then a tensor of the difference of values from the two most recent 4-dimensional location vectors. No additional CNN layer is utilized in this case.
- **Ball Position Input:** A design as similar to the *DishBrain* system's input structure as possible was also examined. For this case, the y-axis of the gameplay environment was divided into 8 equal segments each mimicking one of the sensory electrodes in the biological cultures, and place coding the information about the ball's y-axis position as an integer in the [1, 8] interval. Then, the ball's x-axis position is used as the second element of this input vector being an integer value in [4, 40] similar to the rate coded component of the stimulation applied to the biological cultures. No additional CNN layer is utilized in this design.

The overview of the implemented DQN, A2C, and PPO algorithms are represented in Supplementary Materials A.4 (see Algorithms 1, 2, and 3).

All the deep RL implementations run on a 2.3 GHz Quad-Core Intel Core i5. PyTorch 1.8.1 was used to build neural network blocks and Open AI Gym environment to define our game environment represented by a  $40 \times 40$  pixel grayscale image. In the training phase of all RL algorithms, every algorithm was run for 150 random seeds and a total number of 70 episodes for each seed. These seeds imply 150 different neural networks trained separately, resembling 150 different recorded cultures. In this work, we report the average value of each metric among all seeds.

### 4.3 Connectivity Network Construction

First, we grouped the activity of each recorded channel into bins of spikes, with a set length. In this study, we used a window of 100ms, with a 50ms sliding window to sort spikes into bins. A network matrix using functional connectivity – defined as the zero-lag Pearson correlations – of each Gameplay or Rest session recording was constructed across all bins. Then, the number of nodes, which represents the number of active electrodes during one full recording, the number of edges, which represents the Pearson Correlations between pairs of nodes, density, which represents the ratio between the number of connections and the number of possible connections in a fully-connected graph, the mean

<sup>&</sup>lt;sup>1</sup>We also experimented with an alternative design where the input consisted of a stack of the four most recent frames for all algorithms. However, this modification led to a noticeable decline in the performance of all the methods because it failed to capture the sense of motion between frames.

participation coefficient (pcoeff), which represents the diversity of intermodular connections of individual nodes [33], average weight or degree of each node, modularity index, which represents the degree to which the network may be subdivided into modules, clustering coefficient which represents the fraction of node's neighbors that are neighbors of each other, max betweenness, which represents the maximum value of betweenness centrality that reflects the number of nodes that participate in a large number of shortest paths, and the characteristic path length which represents the average shortest path length in the network were calculated.

In the realm of unraveling information from intricate and high-dimensional networks, a significant recent focus has been directed towards the exploration of obtaining network embeddings in lower dimensions. The central aim of this approach is to obtain vector representations for individual nodes within the network, capturing valuable and meaningful insights [34–36].

Hence, in this work, we first employed a dimensionality reduction algorithm to both enhance the computational efficiency of subsequent data analysis and improve data interoperability [37]. To determine which areas of the network were most responsible for learning, we first embedded the spiking activity of all the recorded channels in a lower-dimensional space using t-SNE [38] method. To evaluate the effectiveness of this metric in capturing learning-related network structures, we divided recording sessions in half before implementing dimensionality reduction. Results presented in Figure 6.j. showcase t-SNE outcomes with color-coded distinctions for the initial and latter portions of 20-minute *Gameplay* and 10-minute *Rest* sessions across three samples.

Furthermore, in complex neural networks, only a subset of neurons becomes active at any given moment, and many do not exhibit distinct action potentials. Recent findings highlight the development of specialized, selective, and abstract response properties in the cortex [39], underscoring the significance of sparse activity and connectivity patterns. These patterns conserve energy and enhance computational efficiency [40], highlighting the redundancy inherent in assessing individual neuron firing patterns. The brain's capacity to encode and process information depends on the coordinated activity of neuronal populations, often conveying redundant or highly correlated signals.

In light of these collective behaviors observed in neuronal networks, our objective was to enhance the reduction of computational complexity when studying these neuronal populations, all the while maintaining the dynamic properties of the network. We devised a method to pinpoint a subset of recorded channels that likely monitored the neuronal populations especially attuned to the ongoing task. This subset enables the identification of key neurons characterizing the network's behavior during *Gameplay*, to more efficiently study the (macroscopic) of this smaller and interpretable network.

Hence, instead of utilizing all of the 1024 channels, we extracted a subset of representative channels following a K-medoid clustering algorithm, creating 30 clusters, and extracting the corresponding "medoids" as the representative channel for each cluster. Selecting K > 30 clusters did not significantly

improve the clustering accuracy measured by the Davies-Bouldin index. Next, by utilizing these low-dimensional representations, we recreated the functional connectivity matrices from these 30 channels as the nodes and the edges between these nodes represented by Pearson correlations as described previously. Only edges with an absolute Pearson correlation above 0.7 were kept. We then explored the patterns of the previously introduced macroscopic neuronal network dynamics during learning. Details of the utilized pipeline to construct these connectivity networks are outlined in Supplementary Materials A.6 and Extended Data Figure B10.

After constructing the connectivity networks, we aimed to examine their temporal evolution in both *Gameplay* and *Rest*. To achieve this, we divided each recording session into 2-minute windows and evaluated the change in edge weights as the network evolved over those windows.

# 4.4 Data Availability

All data generated for or used within this manuscript have been deposited at Open Science Framework (OSF) and are publicly available here: https://osf.io/cnpzf/?view\_only=a33b7083f78e4c55a20b6c021a695a4a.

# 4.5 Code Availability

All code for deep reinforcement learning models or used for data analysis to generate the results in this manuscript have been deposited at Open Science Framework (OSF) and are publicly available via https://osf.io/cnpzf/?view\_only=a33b7083f78e4c55a20b6c021a695a4a.

# 4.6 Supplementary information

Supplementary Materials; Extended Data; Tables S1 - S3

# 4.7 Acknowledgments

The authors thank and acknowledge Dr Haytham Fayek, Dr Hon Weng Chong and Mr Amitesh Gaurav for their input and advice on the manuscript and experimental design.

# 4.8 Competing interests

B.J.K., F.H., A.L., and M.K. were contracted or employed by Cortical Labs during the course of this research. B.J.K. has shares in Cortical Labs and an interest in patents related to this work. There are no other competing interests to declare.

# 4.9 Author contributions

B.J.K., M.K., and F.H. conceived and designed the work. M.K. developed the models and performed the experiments under the guidance of B.J.K.

### Springer Nature 2021 $IAT_EX$ template

### 22 Biological Neurons vs Deep Reinforcement Learning

F.H. and M.K. analysed the data and conducted method comparisons. M.K., F.H., A.L. and B.J.K contributed to materials and the analysis tool. A.P. and A.R. conducted additional analysis. M.K., F.H., and B.J.K. drafted the initial manuscript. All authors contributed to reviewing the manuscript.

# References

•

- [1] Neftci, E. O. & Averbeck, B. B. Reinforcement learning in artificial and biological systems 1 (3), 133–143. URL http://www.nature.com/articles/ s42256-019-0025-4. https://doi.org/10.1038/s42256-019-0025-4.
- [2] Lake, B. M., Ullman, T. D., Tenenbaum, J. B. & Gershman, S. J. Building machines that learn and think like people 40, e253. URL https://www.cambridge.org/core/product/ identifier/S0140525X16001837/type/journal\_article. https://doi.org/10. 1017/S0140525X16001837.
- [3] Hassabis, D., Kumaran, D., Summerfield, C. & Botvinick, M. Neuroscience-inspired artificial intelligence 95 (2), 245–258. URL https://linkinghub.elsevier.com/retrieve/pii/S0896627317305093. https://doi.org/10.1016/j.neuron.2017.06.011.
- [4] Richards, B. A. *et al.* A deep learning framework for neuroscience **22** (11), 1761–1770. URL https://www.nature.com/articles/s41593-019-0520-2. https://doi.org/10.1038/s41593-019-0520-2.
- [5] Hasson, U., Nastase, S. A. & Goldstein, A. Direct fit to nature: An evolutionary perspective on biological and artificial neural networks 105 (3), 416–434. URL https://linkinghub.elsevier.com/retrieve/pii/ S089662731931044X. https://doi.org/10.1016/j.neuron.2019.12.002.
- [6] Kagan, B. J. *et al.* In vitro neurons learn and exhibit sentience when embodied in a simulated game-world. *Neuron* (2022).
- [7] Sutton, R. S. & Barto, A. G. Reinforcement learning: An introduction (MIT press, 2018).
- [8] Hessel, M. et al. Rainbow: Combining improvements in deep reinforcement learning. ArXiv abs/1710.02298 (2017).
- [9] Moravčík, M. et al. Deepstack: Expert-level artificial intelligence in headsup no-limit poker. Science 356 (6337), 508–513 (2017).
- [10] Jaderberg, M. *et al.* Human-level performance in first-person multiplayer games with population-based deep reinforcement learning. arXiv. *arXiv* preprint arXiv:1807.01281 (2018).
- [11] Silver, D. et al. Mastering chess and shogi by self-play with a general reinforcement learning algorithm. arXiv preprint arXiv:1712.01815 (2017)

- 24 Biological Neurons vs Deep Reinforcement Learning
- [12] Silver, D. et al. Mastering the game of go without human knowledge. nature 550 (7676), 354–359 (2017) .
- [13] Silver, D. et al. A general reinforcement learning algorithm that masters chess, shogi, and go through self-play. *Science* **362** (6419), 1140–1144 (2018).
- [14] Mnih, V. et al. Human-level control through deep reinforcement learning. nature 518 (7540), 529–533 (2015).
- [15] Tsividis, P. A., Pouncy, T., Xu, J. L., Tenenbaum, J. B. & Gershman, S. J. Human learning in atari (2017).
- [16] Marcus, G. Deep learning: A critical appraisal. arXiv preprint arXiv:1801.00631 (2018).
- [17] Gibney, E. et al. This ai researcher is trying to ward off a reproducibility crisis. Nature 577 (7788), 14–14 (2020).
- [18] Kirkpatrick, J. et al. Overcoming catastrophic forgetting in neural networks 114 (13), 3521–3526. URL https://pnas.org/doi/full/10.1073/ pnas.1611835114. https://doi.org/10.1073/pnas.1611835114.
- [19] Fan, L. & Glynn, P. W. The fragility of optimized bandit algorithms. URL http://arxiv.org/abs/2109.13595. 2109.13595[cs,math,stat].
- [20] Mousavi, S. S., Schukat, M. & Howley, E. Bi, Y., Kapoor, S. & Bhatia, R. (eds) Deep reinforcement learning: An overview. (eds Bi, Y., Kapoor, S. & Bhatia, R.) Proceedings of SAI Intelligent Systems Conference (IntelliSys) 2016, 426–440 (Springer International Publishing, Cham, 2018).
- [21] Freitag, C. et al. The real climate and transformative impact of ICT: A critique of estimates, trends, and regulations 2 (9), 100340. URL https://www.sciencedirect.com/science/article/pii/S2666389921001884. https://doi.org/10.1016/j.patter.2021.100340.
- [22] Whittington, J. C. & Bogacz, R. Theories of error back-propagation in the brain 23 (3), 235–250. URL https://linkinghub.elsevier.com/retrieve/ pii/S1364661319300129. https://doi.org/10.1016/j.tics.2018.12.005.
- [23] Hamid, A. A. et al. Mesolimbic dopamine signals the value of work
   19 (1), 117–126. URL http://www.nature.com/articles/nn.4173. https://doi.org/10.1038/nn.4173.
- [24] Costa, V., Dal Monte, O., Lucas, D., Murray, E. & Averbeck, B. Amygdala and ventral striatum make distinct contributions to reinforcement learning 92 (2), 505–517. URL https://linkinghub.elsevier.com/retrieve/

pii/S0896627316305840. https://doi.org/10.1016/j.neuron.2016.09.025 .

- [25] Friston, K. J., Daunizeau, J. & Kiebel, S. J. Reinforcement learning or active inference? 4 (7), e6421. URL https://dx.plos.org/10.1371/journal. pone.0006421. https://doi.org/10.1371/journal.pone.0006421.
- [26] Song, Y. et al. Inferring neural activity before plasticity: A foundation for learning beyond backpropagation. bioRxiv 2022–05 (2022).
- [27] Whittington, J. C. & Bogacz, R. An approximation of the error backpropagation algorithm in a predictive coding network with local hebbian synaptic plasticity. *Neural computation* **29** (5), 1229–1262 (2017).
- [28] Tessadori, J., Bisio, M., Martinoia, S. & Chiappalone, M. Modular neuronal assemblies embodied in a closed-loop environment: Toward future integration of brains and machines 6. URL http://journal.frontiersin.org/ article/10.3389/fncir.2012.00099/abstract. https://doi.org/10.3389/fncir. 2012.00099.
- [29] Bakkum, D. J., Chao, Z. C. & Potter, S. M. Spatio-temporal electrical stimuli shape behavior of an embodied cortical network in a goal-directed learning task **5** (3), 310–323. URL http://stacks.iop.org/1741-2552/5/i=3/a=004?key=crossref.2e55c5e1d3b8c9612fd3ab6762195e65. https://doi.org/10.1088/1741-2560/5/3/004.
- [30] Müller, J., Bakkum, D. J. & Hierlemann, A. Sub-millisecond closedloop feedback stimulation between arbitrary sets of individual neurons. *Frontiers in neural circuits* 6, 121 (2013).
- [31] Harrell, E. R., Goldin, M. A., Bathellier, B. & Shulz, D. E. An elaborate sweep-stick code in rat barrel cortex 6 (38), eabb7189. URL https://www. science.org/doi/10.1126/sciadv.abb7189. https://doi.org/10.1126/sciadv. abb7189.
- [32] Kagan, B. J. et al. The technology, opportunities and challenges of synthetic biological intelligence. Biotechnology Advances 108233 (2023).
- [33] Rubinov, M. & Sporns, O. Complex network measures of brain connectivity: uses and interpretations. *Neuroimage* 52 (3), 1059–1069 (2010)
- [34] Perozzi, B., Al-Rfou, R. & Skiena, S. Deepwalk: Online learning of social representations, 701–710 (2014).
- [35] Tang, J. et al. Line: Large-scale information network embedding, 1067– 1077 (2015).

- 26 Biological Neurons vs Deep Reinforcement Learning
- [36] Khajehnejad, M. Simnet: Similarity-based network embeddings with mean commute time. *PloS one* 14 (8), e0221172 (2019).
- [37] Khajehnejad, M., Habibollahi, F., Loeffler, A., Kagan, B. & Razi, A. On complex network dynamics of an in-vitro neuronal system during rest and gameplay (2023).
- [38] Van der Maaten, L. & Hinton, G. Visualizing data using t-sne. Journal of machine learning research 9 (11) (2008).
- [39] Wolfe, J., Houweling, A. R. & Brecht, M. Sparse and powerful cortical spikes. *Current opinion in neurobiology* 20 (3), 306–312 (2010).
- [40] Olshausen, B. A. & Field, D. J. Sparse coding of sensory inputs. Current opinion in neurobiology 14 (4), 481–487 (2004).
- [41] Habibollahi, F., Kagan, B. J., Burkitt, A. N. & French, C. Critical dynamics arise during structured information presentation within embodied in vitro neuronal networks. *Nature Communications* 14 (1), 5287 (2023).
- [42] Jouppi, N. P. *et al.* A domain-specific supercomputer for training deep neural networks **63** (7), 67–78. URL https://doi.org/10.1145/3360307. https://doi.org/10.1145/3360307.
- [43] Buchanan, M. Organoids of intelligence. Ph.D. thesis, Nature Publishing Group (2018).
- [44] Bastos, A. et al. Visual areas exert feedforward and feedback influences through distinct frequency channels 85 (2), 390–401. URL https: //linkinghub.elsevier.com/retrieve/pii/S089662731401099X. https://doi. org/10.1016/j.neuron.2014.12.018.
- [45] Hinton, G. The forward-forward algorithm: Some preliminary investigations. arXiv preprint arXiv:2212.13345 (2022).
- [46] Felleman, D. J. & Van Essen, D. C. Distributed hierarchical processing in the primate cerebral cortex. *Cerebral cortex (New York, NY: 1991)* 1 (1), 1–47 (1991).
- [47] Hopfield, J. J. Neural networks and physical systems with emergent collective computational abilities. *Proceedings of the national academy of sciences* **79** (8), 2554–2558 (1982).
- [48] Rao, R. P. & Ballard, D. H. Predictive coding in the visual cortex: a functional interpretation of some extra-classical receptive-field effects. *Nature neuroscience* 2 (1), 79–87 (1999).

- [49] Friston, K. A theory of cortical responses. Philosophical transactions of the Royal Society B: Biological sciences 360 (1456), 815–836 (2005).
- [50] de Wit, L., Machilsen, B. & Putzeys, T. Predictive coding and the neural response to predictable stimuli. *Journal of Neuroscience* **30** (26), 8702– 8703 (2010).
- [51] Chua, K., Calandra, R., McAllister, R. & Levine, S. Deep reinforcement learning in a handful of trials using probabilistic dynamics models. *Advances in neural information processing systems* **31** (2018).
- [52] Lee, S. Y., Sungik, C. & Chung, S.-Y. Sample-efficient deep reinforcement learning via episodic backward update. Advances in Neural Information Processing Systems 32 (2019).
- [53] Franke, J. K., Köhler, G., Biedenkapp, A. & Hutter, F. Sample-efficient automated deep reinforcement learning. arXiv preprint arXiv:2009.01555 (2020).
- [54] Stooke, A. & Abbeel, P. Accelerated methods for deep reinforcement learning. arXiv preprint arXiv:1803.02811 (2018).
- [55] Smirnova, L. et al. Organoid intelligence (oi): the new frontier in biocomputing and intelligence-in-a-dish. Frontiers in Science 1, 1017235 (2023)
- [56] Ruaro, M. E., Bonifazi, P. & Torre, V. Toward the neurocomputer: image processing and pattern recognition with neuronal cultures. *IEEE Transactions on Biomedical Engineering* 52 (3), 371–383 (2005).
- [57] Arulkumaran, K., Deisenroth, M. P., Brundage, M. & Bharath, A. A. Deep reinforcement learning: A brief survey. *IEEE Signal Processing Magazine* 34 (6), 26–38 (2017).
- [58] Schulman, J., Wolski, F., Dhariwal, P., Radford, A. & Klimov, O. Proximal policy optimization algorithms. arXiv preprint arXiv:1707.06347 (2017).
- [59] Bellman, R. & Kalaba, R. Dynamic programming and statistical communication theory. Proceedings of the National Academy of Sciences 43 (8), 749–751 (1957).
- [60] Keskar, N. S., Mudigere, D., Nocedal, J., Smelyanskiy, M. & Tang, P. T. P. On large-batch training for deep learning: Generalization gap and sharp minima. arXiv preprint arXiv:1609.04836 (2016).

- [61] Renart, A., Brunel, N. & Wang, X.-J. Mean-field theory of irregularly spiking neuronal populations and working memory in recurrent cortical networks. *Computational neuroscience: A comprehensive approach* 431– 490 (2004).
- [62] Baspinar, E., Schülen, L., Olmi, S. & Zakharova, A. Coherence resonance in neuronal populations: Mean-field versus network model. *Physical Review E* 103 (3), 032308 (2021).
- [63] Bick, C., Goodfellow, M., Laing, C. R. & Martens, E. A. Understanding the dynamics of biological and neural oscillator networks through exact mean-field reductions: a review. *The Journal of Mathematical Neuroscience* **10** (1), 9 (2020).
- [64] La Camera, G. in The mean field approach for populations of spiking neurons 125–157 (Springer, 2021).
- [65] Isomura, T. & Friston, K. Reverse-engineering neural networks to characterize their cost functions. Neural Computation 32 (11), 2085–2121 (2020).
- [66] Isomura, T., Shimazaki, H. & Friston, K. J. Canonical neural networks perform active inference. *Communications Biology* 5 (1), 55 (2022).
- [67] Friston, K., Da Costa, L., Hafner, D., Hesp, C. & Parr, T. Sophisticated inference. Neural Computation 33 (3), 713–763 (2021). URL https://doi. org/10.1162/neco\_a\_01351. https://doi.org/10.1162/neco\_a\_01351.
- [68] Kaplan, R. & Friston, K. J. Planning and navigation as active inference. Biological Cybernetics 112 (4), 323–343 (2018). URL https://doi.org/10. 1007/s00422-018-0753-2. https://doi.org/10.1007/s00422-018-0753-2.
- [69] Kuchling, F., Friston, K., Georgiev, G. & Levin, M. Morphogenesis as bayesian inference: A variational approach to pattern formation and control in complex biological systems. *Physics of Life Reviews* 33, 88–108 (2020). URL https://www.sciencedirect.com/science/article/ pii/S1571064519300909. https://doi.org/https://doi.org/10.1016/j.plrev. 2019.06.001.
- [70] Tschantz, A., Seth, A. K. & Buckley, C. L. Learning action-oriented models through active inference. *PLOS Computational Biology* 16 (4), 1–30 (2020). URL https://doi.org/10.1371/journal.pcbi.1007805. https://doi.org/10.1371/journal.pcbi.1007805.
- [71] Parr, T. & Friston, K. J. The discrete and continuous brain: From decisions to movement-and back again. Neural computation 30 (29894658), 2319–2347 (2018). URL https://www.ncbi.nlm.nih.gov/pmc/articles/

PMC6115199/. https://doi.org/10.1162/neco\_a\_01102 .

- [72] Isomura, T. Active inference leads to bayesian neurophysiology. Neuroscience Research 175, 38–45 (2022). URL https://www. sciencedirect.com/science/article/pii/S0168010221002595. https://doi. org/https://doi.org/10.1016/j.neures.2021.12.003, constructive Understanding of Multi-scale Dynamism of Neuropsychiatric Disorders.
- [73] Lovejoy, W. S. A survey of algorithmic methods for partially observed markov decision processes. Annals of Operations Research 28 (1), 47–65 (1991). URL https://doi.org/10.1007/BF02055574. https://doi.org/10. 1007/BF02055574.
- [74] Shani, G., Pineau, J. & Kaplow, R. A survey of point-based pomdp solvers. Autonomous Agents and Multi-Agent Systems 27 (1), 1–51 (2013). URL https://doi.org/10.1007/s10458-012-9200-2. https://doi.org/10.1007/s10458-012-9200-2.
- [75] Kaelbling, L. P., Littman, M. L. & Cassandra, A. R. Planning and acting in partially observable stochastic domains. *Artificial Intelligence* 101 (1), 99–134 (1998). URL https://www.sciencedirect.com/ science/article/pii/S000437029800023X. https://doi.org/https://doi.org/ 10.1016/S0004-3702(98)00023-X.
- [76] Paul, A., Sajid, N., Gopalkrishnan, M. & Razi, A. Active inference for stochastic control, 669–680 (Springer, 2021).

# Appendix A Supplementary Materials

# A.1 Cell Culture

Neural cells were cultured either from the cortices of E15.5 mouse embryos or differentiated from human induced pluripotent stem cells via a dual SMAD inhibition (DSI) protocol as previously described [6]. Cells were cultured until plating onto MEA. For primary mouse neurons, this occurred at day-in-vitro (DIV) 0, for DSI cultures this occurred at between DIV 30 - 33 depending on culture development.

## A.2 MEA Setup and Plating

MaxOne Multielectrode Arrays (MEA; Maxwell Biosystems, AG, Switzerland) was used and is a high-resolution electrophysiology platform featuring 26,000 platinum electrodes arranged over an 8 mm2. The MaxOne system is based on complementary meta-oxide-semiconductor (CMOS) technology and allows recording from up to 1024 channels. MEAs were coated with either polyethylenimine (PEI) in borate buffer for primary culture cells or Poly-D-Lysine for cells from an iPSC background before being coated with either 10 µg/ml mouse laminin or 10 µg/ml human 521 Laminin (Stemcell Technologies Australia, Melbourne, Australia) respectively to facilitate cell adhesion. Approximately  $10^6$  cells were plated on MEA after preparation as per [6]. Cells were allowed approximately one hour to adhere to the MEA surface before the well was flooded. The day after plating, cell culture media was changed for all culture types to BrainPhys<sup>™</sup> Neuronal Medium (Stemcell Technologies Australia, Melbourne, Australia) supplemented with 1% penicillin-streptomycin. Cultures were maintained in a low O2 incubator kept at 5% CO2, 5% O2, 36°C and 80% relative humidity. Every two days, half the media from each well was removed and replaced with free media. Media changes always occurred after all recording sessions.

### A.3 DishBrain platform and electrode configuration

The current *DishBrain* platform is configured as a low-latency, real-time MEA control system with on-line spike detection and recording software. The *DishBrain* platform provides on-line spike detection and recording configured as a low-latency, real-time MEA control. The *DishBrain* software runs at 20 kHz and allows recording at an incredibly fine timescale. There is the option of recording spikes in binary files, and regardless of recording, they are counted over a period of 10 milliseconds (200 samples), at which point the game environment is provided with how many spikes are detected in each electrode in each predefined motor region as described below. Based on which motor region the spikes occurred in, they are interpreted as motor activity, moving the 'paddle' up or down in the virtual space. As the ball moves around the play area at a fixed speed and bounces off the edge of the play area and the paddle, the pong game is also updated at every 10ms interval. Once the ball

hits the edge of the play area behind the paddle, one rally of pong has come to an end at which point a 'miss' would be recorded and an unpredictable stimulation would be delivered to the cells. Using a feedback stimulus at a voltage of 150 mV and a frequency of 5 Hz, unpredictable external stimulus could be added to the system. Random stimulation took place at random sites over the 8 predefined input electrodes at random timescales for a period of four seconds, followed by a configurable rest period of four seconds where stimulation paused, then the next rally began.

In contrast, a predictable stimulus feedback is provided when the ball contacts the paddle under the standard stimulus condition. Predictable stimulus feedback involves 75mV stimulation at 100Hz over 100ms occurring when the simulated ball struck the paddle and replaced other sensory information. All 8 stimulation electrodes simultaneously would receive predictable stimulation at this frequency and period. A 'stimulation sequencer' module tracks the location of the ball relative to the paddle during each rally and encodes it as stimulation to one of eight stimulation sites. Each time a sample is received from the MEA, the stimulation sequencer is updated 20,000 times a second, while the game itself runs at 100Hz. After the previous lot of MEA commands has completed, the *DishBrain* system constructs a new sequence of MEA commands based on the information it has been configured to transmit based on both place codes and rate codes. The stimulations take the form of a short square bi-phasic pulse that is a positive voltage, then a negative voltage. This pulse sequence is read and applied to the electrode by a Digital to Analog Converter (or DAC) on the MEA. A real-time interactive version of the game visualizer is available at https://spikestream.corticallabs.com/. Alternatively, cells could be recorded at 'rest' in a gameplay environment where activity was recorded to move the paddle but no stimulation was delivered, with corresponding outcomes still recorded. Using this spontaneous activity alone as a baseline, the gameplay characteristics of a culture were determined. Low level code for interacting with Maxwell API was written in C to minimize processing latencies-so packet processing latency was typically  $<50 \ \mu s$ . High-level code was written in Python, including configuration setups and general instructions for game settings. A 5 ms spike-to-stim latency was achieved, which was substantially due to MaxOne's inbuilt hardware buffering. Figure B1 illustrates a schematic view of Software components and data flow in the *DishBrain* closed loop system.

### A.4 Deep Reinforcement Learning Algorithms

**Deep Q Network (DQN):** The utilized DQN algorithm begins by extracting spatiotemporal features from inputs, such as the movement of the ball in the game of 'Pong'. Multiple fully connected layers are used to process the final feature map, which implicitly encodes the effects of actions. As opposed to traditional controllers that use fixed preprocessing steps, this method can adapt the processing of the state based on changes in the learning signal. An epsilon-greedy algorithm was employed in this work to balance the exploration

and exploitation capabilities of the DQN algorithm.

For the results represented in this manuscript, a comprehensive grid search was conducted within the parameter space of *learning rate* ([0.0001, 0.004]), replay buffer size ([10, 100000]), and the training batch size ([5, 128]) with starting point of 0.0001, 32, 10000, respectively, aiming to identify the optimal parameter configuration. The results presented in this paper are derived from the superior set of hyper-parameters obtained through this search process. As the outcome of this search for the DQN algorithm, we selected *learning rate* = 0.002, replay buffer size = 10000, and batch size = 16 for the results of Figure 2, learning rate = 0.001, replay buffer size = 10000, and batch size = 16 for the results of Figure 3, and learning rate = 0.001, replay buffer size = 10000, and batch size = 32 for the results of Figure 4. Figure B2 illustrates the performance of the DQN algorithm with IMAGE INPUT design in terms of average rally length in several sample points of the mentioned search space. While exploring each hyper-parameter in Figure B2, the remaining pair are set to the same values as the starting point of the search (i.e. *learning rate* =0.0001, batch size = 32, and replay buffer size = 10000).

For additional details on the set of explored hyper-parameters and network architectures, see Table S1.

Algorithm 1 Deep Q Network (DQN) with Experience Replay			
Require:			
1: $\mathcal{D}$ : Replay buffer with size N (Default: 10000)			
2: $\theta$ : Initial network parameters			
3: $\tilde{\theta}$ : Copy of $\theta$			
$\gamma$ : Discount factor (Default: 0.95)			
5: $N_b$ : Training batch size (Default: 16)			
6: $\tilde{N}$ : Target network update frequency (Default: 10)			
7: $x_t$ : Input matrix at time $t$			
3: S: Number of seeds (Default: 150)			
$e_{max}$ : Maximum number of episodes (Default: 70)			
10: for seed $\in \{1, \cdots, S\}$ do			
11: <b>for</b> episode $e \in \{1, \dots, e_{max}\}$ <b>do</b>			
12: Set state $s_1 \leftarrow x_1$ and preprocess $\phi_1 = \phi(s_1)$			
13:   t = 1			
14: while $\phi_t$ is non-terminal <b>do</b>			
15. With probability $\epsilon$ select a random action $a_t$			
16: otherwise select $a_t = max_a Q^*(\phi(s_t), a; \theta)$			
17: Execute action $a_t$ and observe reward $r_t$ and input $x_{t+1}$			
18: Set new state $s_{t+1}$ and preprocess $\phi_{t+1} = \phi(s_{t+1})$			
19: Store transition $(\phi_t, a_t, r_t, \phi_{t+1})$ in $\mathcal{D}$			
20: Sample random minibatch of $N_b$ transitions $(\phi_j, a_j, r_j, \phi_{j+1})$ from $\mathcal{I}$	)		
21: Set $y_j = \begin{cases} r_j & \text{for terminal } \phi_{j+1} \\ r_j + \gamma max_{a'}Q(\phi_{j+1}, a'; \theta) & \text{for non-terminal } \phi_{j+1} \end{cases}$			
22: Perform a gradient descent step on $(y_j - Q(\phi_j, a_j; \theta))^2$			
23: Replace target parameters $\theta \leftarrow \theta$ every $\hat{N}$ steps			
24: $t = t + 1$			
25: end while			
26: end for			
27: end for			
	_		

Advantage Actor-Critic (A2C): In an A2C model, the total reward itself could be represented as a *value* of the state plus the advantage of the action. The value of each policy is learned while following it. The policy gradient can be calculated by knowing the *value* for any state. The policy network is then updated such that the probability of actions with a higher advantage value is increased. Here, the policy network (which returns a probability distribution of actions) is called the *actor*, as it tells the agents what to do. *Critic* is another network that enables the evaluation of the actions to decide whether they were good or not. In this case, policy and value are implemented as separate heads of the network, which transform the output from the common body into either probability distributions or single numbers representing the state's value. Thus, low-level features can be shared between the two networks.

For the results represented in the main paper, a comprehensive grid search was conducted within the parameter space of actor learning rate ([0.0001, 0.004]), critic learning rate ([0.0001, 0.004]), and the training batch size ([5, 128]), to identify the optimal parameter configuration. As the outcome of this search for A2C, we selected actor learning rate = 0.001, 0.0001, 0.003, critic learning rate = 0.001, 0.001, 0.001, and batch size = 32, 32,5 for the results of Figure 2, 3, and 4, respectively. Figure B2 contains the results of this hyper-parameter search for the A2C algorithm with the IMAGE INPUT design in terms of average rally length in several sample points of the mentioned search space. While exploring each hyper-parameter in Figure B2, the remaining pair are set to the same values as the starting point of the search (i.e. actor learning rate =0.0001, batch size = 32, and critic learning rate = 0.001).

Algorithm 2 Advantage Actor-Critic (A2C) **Require:** 1:  $\hat{\theta}_{v}$ : Initial parameter vector for the value net (critic) 2:  $\theta_{\pi}$ : Initial parameter vector for the policy net (actor) 3:  $\gamma$ : Discount factor (Default: 0.95) 4: N: Number of consecutive steps to play current policy in the environment (Default: 5) 5:  $\dot{x}_t$ : Input matrix at time t 6: S: Number of seeds (Default: 150) 7:  $e_{max}$ : Maximum number of episodes (Default: 70) 8: for seed  $\in \{1, \cdots, S\}$  do t = 19: 10: e = 111: repeat  $\partial \theta_{\pi} \leftarrow 0 \text{ and } \partial \theta_{v} \leftarrow 0$ 12. 13.  $t_{start} = t$ Set state  $s_t \leftarrow x_t$  and preprocess  $\phi_t = \phi(s_t)$  $14 \cdot$ 15:repeat Select  $a_t$  according to  $\pi(a_t \mid \phi_t; \theta)$ 16: Execute action  $a_t$  and observe reward  $r_t$  and input  $x_{t+1}$ 17:Set new state  $s_{t+1}$  and preprocess  $\phi_{t+1} = \phi(s_{t+1})$ 18: 19:  $t \leftarrow t + 1$ **until**  $\phi_t$  is terminal **or**  $t - t_{start} = N$ 20:  $R = \begin{cases} 0 & \text{for terminal } \phi_t \\ V(\phi_t; \ \theta_v) & \text{for non-terminal } \phi_t \end{cases}$ 21: for  $i \in \{t-1, \cdots, t_{start}\}$  do 22:  $R \leftarrow r_i + \gamma R$ 23:Accumulate the policy gradients:  $\partial \theta_{\pi} \leftarrow \partial \theta_{\pi} + \nabla_{\theta} \log \pi(a_i \mid \phi_i; \theta) (R - \theta_i)$  $24 \cdot$  $V(\phi_i, \theta_v))$ Accumulate the value gradients:  $\partial \theta_v \leftarrow \partial \theta_v + \frac{\partial \left(R - V(\phi_i, \theta_v)\right)^2}{\partial \theta}$ 25:end for 26:27:Update  $\theta_{\pi}$  and  $\theta_{v}$  using  $\partial \theta_{\pi}$  and  $\partial \theta_{v}$ , respectively. if  $\phi_t$  is terminal then 28:29:  $e \leftarrow e + 1$ end if 30until  $e > e_{max}$  $31 \cdot$ 32: end for

**Proximal Policy Optimization (PPO):** PPO models are a family of policy gradient methods for reinforcement learning. The PPO method uses a slightly different training procedure: An extended set of samples is taken from the environment, and then the advantage is estimated for the whole set or sequence of samples before several epochs of training are performed To estimate policy gradients, instead of using the gradient of action probabilities, the PPO method uses a different objective: the ratio between the new and the old policy scaled by the advantages.

Once more, for the results represented in the main paper, we used the outcome of a grid search for the PPO algorithm in the same space as A2C above and utilized *actor learning rate* = 0.003, 0.0001, 0.001, *critic learning rate* = 0.003, 0.0001, 0.001, *and batch size* = 16, 16, 32 to generate the results of Figure 2, 3, and 4, respectively.

Figure B2 represents the performance of the PPO algorithm with the IMAGE

INPUT design in terms of average rally length in several sample points of the mentioned search space. While exploring each hyper-parameter in Figure B2, the remaining pair are set to the same values as the starting point of the search (i.e. *actor learning rate* = 0.0001, *batch size* = 32, and *critic learning rate* = 0.0001).

#### Algorithm 3 Proximal Policy Optimization (PPO)

#### **Require:**

1:  $\theta$ : Initial policy parameter vector 2:  $\epsilon$ : Clipping threshold (Default: 0.2) 3:  $\gamma$ : Discount factor (Default: 0.95) 4:  $\lambda$ : GAE parameter (Default: 1) 5: N: Number of consecutive steps to play current policy in the environment (Default: 32) 6:  $x_t$ : Input matrix at time t 7: S: Number of seeds (Default: 150) 8:  $e_{max}$ : Maximum number of episodes (Default: 70) 9: for seed  $\in \{1, \cdots, S\}$  do 10: t = 111: e = 112: repeat  $t_{start} = t$ 13:Set state  $s_t \leftarrow x_t$  and preprocess  $\phi_t = \phi(s_t)$  $14 \cdot$  $15 \cdot$ repeat Select  $a_t$  according to  $\pi(a_t \mid \phi_t; \theta)$ 16: Execute action  $a_t$  and observe reward  $r_t$  and input  $x_{t+1}$ 17:Set new state  $s_{t+1}$  and preprocess  $\phi_{t+1} = \phi(s_{t+1})$ 18:  $t \leftarrow t + 1$ 19: **until**  $\phi_t$  is terminal **or**  $t - t_{start} = N$ 20:Collect set of partial trajectories  $\mathcal{D}$  on current policy  $\pi$ 21:Estimate Advantages  $\hat{A}_t^{\pi} = \sigma_t + (\gamma \lambda) \sigma_{t+1} + \dots + (\gamma \lambda)^{N-t-1} \sigma_{N-1}$ , where 22: $\sigma_t = r_t + \gamma V(\phi_{t+1}) - V(\phi_t)$  $\theta \leftarrow \operatorname{argmax}_{\theta} \mathcal{L}_{\theta}^{CLIP}(\theta)$ 23:where  $\mathcal{L}_{\theta}^{CLIP}(\theta) = \mathbb{E}_{\tau \sim \pi} \left[ \sum_{t=0}^{T} \left[ \min(r_t(\theta) \hat{A}_t^{\pi}, clip(r_t(\theta), 1 - \epsilon, 1 + \epsilon) \right] \right]$ 24: $\epsilon \hat{A}_t^{\pi}$ **if**  $\phi_t$  is terminal **then** 25:26: $e \leftarrow e + 1$ end if  $27 \cdot$ until  $e > e_{max}$ 28. 29: end for

Figure B7 illustrates the mean total reward of the RL algorithms using the same hyper-parameter sets as in Figure 2 for an extended training period of 11000 game episodes. These results demonstrate successful learning and improved performance over an extended number of training episodes for all three algorithms.

#### Springer Nature 2021 LATEX template

#### 36 Biological Neurons vs Deep Reinforcement Learning

Table S1 Experimented Hyper-parameter and network architecture details

Hyper-parameter	Algorithm	Tested Values
$Conv_1$ size	DQN,A2C,PPO	(16 × 16) <sup>*</sup> , (64 × 64)
$Conv_2$ size	DQN,A2C,PPO	<b>(32</b> × <b>32)</b> , (64 × 64)
Conv <sub>3</sub> size	DQN,A2C,PPO	<b>(32</b> × <b>32)</b> , (64 × 64)
last hidden layer size	DQN,A2C,PPO	{100, 256, <b>512</b> }
number of seeds	DQN,A2C,PPO	150
kernel size	DQN,A2C,PPO	$\{5, 4\}$
stride	DQN,A2C,PPO	2
batch size	DQN,A2C,PPO	[5,128]
discount factor	DQN,A2C,PPO	$\{0.85,  0.95,  0.99,  0.999\}$
learning rate	DQN	[0.0001,  0.004]
replay buffer size	DQN	[10, 100000]
actor-learning rate	A2C,PPO	[0.0001,  0.004]
critic-learning rate	A2C,PPO	[0.0001,  0.004]
clipping threshold	PPO	$\{0.1,  0.2,  0.3\}$
num of epochs	PPO	$\{5,  8,  10\}$

\* The parameter values jointly chosen for all algorithms are highlighted in bold.

### A.5 Additional Hyper-parameter Exploration

#### Effect of Batch Size on Deep RL Algorithm Performances:

From a technical standpoint, there exist no foolproof techniques for identifying the ideal hyper-parameter configuration for training deep RL algorithms. In addition, the batch size has an impact on the convergence rate of the prediction network, with smaller batch sizes resulting in faster convergence and well-known degradation in model quality and generalization abilities that can occur with increased batch sizes [60]. As such, originally we aimed to select batch sizes that would converge within sample numbers comparable to the training period of biological cultures while attempting to prioritize computational efficiency, which is a significant area of interest in this study. Hence, opting for large batch sizes may significantly slow down the model convergence and would not confer any benefit to the RL algorithms under investigation.

Figures B3, B4, and B5 investigate the impact of changing batch sizes utilizing the IMAGE INPUT design by incorporating batch sizes of 8, 16, 32, and 64 while keeping the rest of the hyper-parameters in each algorithm fixed at default levels similar to Figure B2 (i.e. *learning rate* = 0.0001, *batch size* = 32, and *replay buffer size* = 10000 for DQN and *actor learning rate* = 0.0001, *batch size* = 32, and *critic learning rate* = 0.001 for A2C and PPO).

In general, we observed some quantitative changes in outcome metrics when varying the batch size for these algorithms, but these adjustments did
not alter the ultimate conclusions of our work. Focusing on the quality of learning in each group and the comparison of sample efficiency, both of these were unaffected or in some cases worsened by increasing the batch size. Specifically, when examining the statistical significance of metric changes during the first 5 minutes versus the last 15 minutes of training and overall relative improvement, increased batch size did not appear to significantly impact the resulting sample efficiency in any of the algorithms as seen in Extended Data Figure B6.

In some cases, these results illustrate an unwanted trend in the main metrics of interest when increasing the batch size above certain levels. For instance, an increasing % of aces in the DQN and PPO algorithms, decreasing average rally length in PPO, and decreasing % of long rallies in both A2C and PPO algorithms are observed which may eventually prevent the model from converging to the optima. This suggests that if the comparison were to be extended to a larger number of episodes for all groups, the increase in batch size would not necessarily yield improved performances, as evidenced by the undesirable trend observed in the aforementioned metrics (Extended Data Figures B3, B4, and B5). Notably, this may occur due to the fact that larger batch sizes make larger gradient steps than smaller batch sizes for the same number of samples seen and the update is heavily dependent on the specific samples drawn from the dataset. Conversely, a small batch size leads to updates that are more consistent in size, with the size of the update being only weakly dependent on which particular samples are selected from the dataset. In conclusion, it is possible that in deep neural networks, optimal weight configurations are located far from the initial weights. Hence, averaging the loss function over large batch sizes may not allow the model to explore a large enough space to reach the optimal weight configurations within the same number of training epochs.

#### Effects of Adding Hidden Layers on DQN Performance:

To evaluate the effect of adding extra hidden layers on the performance of BALL POSITION INPUT and PADDLE&BALL POSITION INPUT designs to the DQN algorithm, we implemented them by adding 2 additional hidden layers before the output layer and incorporating a batch size = 32. Extended Data Figure B8 shows the outcomes of these adjustments.

This further analysis revealed that although certain metrics exhibited qualitative and quantitative changes in their trends, the overall sample efficiency performance remained unaffected and even worsened with the inclusion of additional hidden layers. For example, we noted a degradation and an unwanted decreasing trend in the DQN's performance in the % of long rallies for the PADDLE&BALL POSITION INPUT design. This resulted in the MCC group significantly outperforming DQN PADDLE&BALL POSITION INPUT design in terms of % of long Rallies during the second 15 minutes. The performance of DQN in terms of average rally length was also deteriorated by the addition of

these layers. On the other hand, MCC no longer demonstrated a significantly superior performance in terms of % of aces by the addition of hidden layers to the PADDLE&BALL POSITION INPUT design. While some level of improvement was detected in the DQN group with the BALL POSITION INPUT design (specifically in the % of aces achieved) by the addition of the extra layers, overall performance in all 3 metrics was still inferior to those of the biological cultures in all the metrics. Specifically as illustrated in Extended Data Figure B9, the HCC group still demonstrated significant outperformance compared to the DQN PADDLE&BALL POSITION INPUT and BALL POSITION INPUT designs in terms of relative improvement. The relative improvement in both of the PADDLE&BALL POSITION INPUT and BALL POSITION INPUT designs showed a decay compared to the results reported in the main text, where this level of outperformance of MCC over DQN was not observed in the absence of hidden layers.

The observed deteriorated performance in terms of relative improvement in the PADDLE&BALL POSITION INPUT design may be attributed to decreased generalization capabilities and higher variance resulting from the introduction of additional hidden layers. Because, for simpler tasks, a smaller network with fewer hidden layers might be sufficient to achieve good performance, and adding more layers could lead to overfitting. Thereby, this declined performance in the relative improvement as well as the low dimensionality of the input information in these designs combined with the faster computational performance of the algorithm with fewer hidden layers can justify the use of the shallower design for comparison reasons.

#### A.6 Network Construction

Recording neuronal spiking activities occurred across 1024 HD-MEA channels during 285 Gameplay and 147 Rest sessions. Due to the extended duration of recordings at a 20 kHz sampling frequency, the resulting time series for Gameplay sessions became notably lengthy. In the context of extracting information from dense and high-dimensional networks, recent emphasis has centered on acquiring network embeddings in lower dimensions. The primary goal of this approach is to obtain vector representations for individual nodes within the network, encapsulating valuable insights [34–36]. Therefore, in this study, we initially employed dimensionality reduction algorithms to enhance computational efficiency for subsequent data analysis and improve data interpretability. This approach also facilitated the revelation of latent data structures not immediately evident in the original high-dimensional space. We utilized t-SNE [38] to generate 2D representations for both Rest and Gameplay data.

Previous studies have extensively utilized simplified models of interconnected neural populations, employing mean-field approximations. These models effectively retain the dynamic properties of the original neural network while significantly accelerating simulation speeds by several orders of magnitude [61–64]. Furthermore, in complex neural networks, only a fraction of neurons fire at any given time, and many do not exhibit clear action potentials. Recent evidence highlights the emergence of specialized, selective, and abstract response properties in the cortex [39], underscoring the significance of sparse activity and connectivity patterns. These patterns conserve energy and optimize computational capacity [40], emphasizing the redundancy in evaluating individual neuron firing patterns. The brain's capacity to encode and process information depends on the concerted action of neuronal populations, often conveying redundant or highly correlated signals. Given these collective behaviors observed in neuronal networks, our objective was to advance the reduction of computational complexity when studying large neuronal populations while still preserving the dynamic properties of the network.

We developed a methodology to identify a subset of recorded channels that likely monitored neuronal populations specifically tuned to the ongoing task. This subset facilitates the identification of key neurons that characterize the network's behavior during Gameplay, allowing for a more efficient study of the macroscopic aspects of this smaller and interpretable network. To establish a consistent subset of channels across all neuronal cultures, we employed Tucker decomposition, utilizing higher-order orthogonal iteration, on the tensor data derived from the 248 Gameplay sessions in the lower-dimensional embedding space. The resulting  $1024 \times 3$  tensor served as a concise representation, capturing underlying patterns and structures. Using this tensor, we identified representative channels by applying the K-medoid clustering algorithm, creating 30 clusters and extracting the corresponding 'medoids' for each cluster. Attempts with a higher value of K did not significantly improve clustering accuracy, as measured by the Davies-Bouldin index. Subsequently, a network matrix was constructed using functional connectivity, defined as zero-lag Pearson correlations, for each Gameplay or Rest session recording. The matrix had these 30 channels as nodes, and the edges between them represented functional connectivity. Only edges with Pearson correlation absolute values above 0.7 were retained.

Figure B10 is a schematic illustration of the proposed in vitro network construction framework in this study.

#### A.7 Active Inference Agent

While RL algorithms use back-propagation, it has been argued that this method is likely too inefficient to function within biological systems. Therefore, we attempted to evaluate the sample efficiency of more biologically inspired algorithms, by implementing a counterfactual learning active inference agent [65, 66]. Our preliminary findings show that one can use a generic active inference agent which can then mimic the performance of the DishBrain system depending on additional parameters such as memory.

The active inference framework is a formal way of modelling the behaviour of self-organising systems that interface with the external world and maintain a consistent form over time [67-69]. The framework assumes that agents embody generative models of the environment they interact with, on which they base

their behaviour [70, 71]. A recent active inference scheme is shown to be mathematically equivalent to a particular class of neural networks accompanied by some neuromodulations of synaptic plasticity [65, 66]. It uses counterfactual learning (CL) to accumulate a measure of risk over time based on feedback from the environment. Subsequent work that validates this scheme experimentally using *in vitro* neural networks has also appeared recently [72]. Of particular note, the training schematic for the DishBrain system was inspired by implications from theory on active inference via the Free Energy Principle, making it the most suitable algorithm to compare here [6]. Here, we focus on generative models in the form of Partially Observable Markov Decision Processes (POMDPs) for their simplicity and ubiquitous use in the optimal control literature [73–75].

Gameplay performance of these agents with two different memory horizons of 3 (CL(3)) and 7 (CL(7)) is summarised in Figure B11. We see that the CL(7) agents perform at par and in some cases better than the HCC group and are the only group where the HCC has no significant outperformance over them in terms of the relative improvement in time (see Figure B11.h). However, this is not the case for CL(3) agents which have a smaller memory horizon. While further exploring this active inference framework is out of scope for this paper, it does highlight the value of using biologically inspired algorithms in terms of sample efficiency.

#### Generative model of the pong game environment:

Assuming agents have a discrete representation of their surrounding environment, we turn to the POMDP framework [75]. POMDPs offer a fairly expressive structure to model discrete state-space environments where parameters can be expressed as tractable categorical distributions. The POMDP-based generative model can be formally defined as a tuple of finite sets  $(S, O, U, \mathbb{B}, \mathbb{A})$ :

In a POMDP, the hidden states (s) generate observations (o) through the likelihood mapping (A) in the form of a categorical distribution,  $P(o_{\tau}|s_{\tau}) = Cat(A \times s_{\tau})$ . B is a collection of square matrices  $\mathbb{B}_u$ , where  $\mathbb{B}_u$  represents transition dynamics  $P(s_t|s_{t-1}, u_{t-1} = u)$ : The transition matrix (B) determines the dynamics of s given the agent's action u as  $P(s_t|s_{t-1}, u_{t-1}) = Cat(\mathbb{B}_{u_{t-1}} \times s_{t-1})$ . In  $[A \times s_{\tau}]$  and  $[\mathbb{B}_{u_{\tau}} \times s_{\tau}]$ ,  $s_{\tau}$  is represented as a one-hot vector that is multiplied through regular matrix multiplication <sup>2</sup>. The Markovianity of POMDPs means that state transitions are independent of history (i.e. state  $s_t$  only depends upon the state-action pair  $(s_{t-1}, u_{t-1})$  and not  $s_{t-2}$ ,  $u_{t-2}$  etc.).

The generative model can be summarised as follows,

$$P(o_{1:t}, s_{1:t}, u_{1:t}) = P(\mathbb{A})P(\mathbb{B})P(\mathbb{D})P(\mathbb{E})\prod_{\tau=1}^{t} P(o_{\tau}|s_{\tau}, \mathbb{A})\prod_{\tau=2}^{t} P(s_{\tau}|s_{\tau-1}, u_{\tau-1}, \mathbb{B})$$
(A1)

<sup>&</sup>lt;sup>2</sup>One-hot is a group of bits among which the legal combinations of values are only those with a single high (1) bit and all the others low (0). Here, the bit (1) is allocated to the state  $s = s_{\tau}$ 

So, from the agent's perspective, when encountering a stream of observations in time, such as  $(o_1, o_2, o_3, ..., o_t)$ , as a consequence of performing a stream of actions  $(u_1, u_2, u_3, ..., u_{t-1})$ , the generative model quantitatively couples and quantifies the causal relationship from action to observation through some assumed hidden states of the environment. These are called 'hidden' states because, in POMDPs, the agent cannot observe them directly. Based on this representation, an agent can now attempt to optimise its actions to keep receiving preferred observations.

The generative model structure used explicitly for the pong game environment is summarised below:

- x-axis location of the ball: Communicated to DishBrain using a stimulation between 4-40 HZ, i.e. 37 states.
- y-axis location of the ball: Communicated to DishBrain through 8 sensory electrodes, i.e. 8 states.
- y-axis location of the paddle: Assumed to be part of DishBrain's generative model as control is exerted, i.e. 8 states.
- Structure: State Space = 37\*8\*8 states, Action Space = {Up, Down, Stav}

#### Counterfactual learning algorithm:

In the counterfactual variant of active inference, the agent learns a state-action mapping  $\mathbb{C}_{\mathbb{P}}$ . For the exact form of the generative model and free energy, refer to [65]. This state-action mapping is learned using a 'Risk' parameter  $\Gamma(t)$ using the update equation as given in [65] as:

$$\mathbb{C}_P \leftarrow \mathbb{C}_P + t \ \langle (1 - 2 \ \Gamma(t)) \langle u_t \otimes s_{t-1} \rangle \rangle. \tag{A2}$$

Here,  $\langle \cdot \rangle$  refers to the average over time, and  $\otimes$  is the Kronecker-product operator. Given the state-action mapping  $\mathbb{C}_{P}$ , agent samples actions from the distribution,

$$P(u|s)_{CL} = \sigma \left( \ln \ \mathbb{C}_P \cdot s_{t-1} \right). \tag{A3}$$

For the complete model, refer to [65]. The free parameter in our model is the number of past instances (of state-action pairs) the agent stores in memory use in every time-step to learn  $\mathbb{C}_P$  in Eq.A2. In the article, we use active inference agents with memory horizons of 3 and 7.

The functional form of  $\Gamma(t)$  used in the simulations of this work is:

$$\Gamma(t)_{prior} = 0.55 \tag{A4}$$

The value of 0.55 corresponds to a bias of "higher risk" in the CL method. An initial value greater than 0.5 is necessary to enable learning. For updating

 $\Gamma$ , we use the equation,

$$\Gamma(t) \leftarrow \Gamma(t) - \frac{1}{T_{goal} - t}.$$
 (A5)

Here,  $T_{goal}$  is when the agent reached the goal state (received a positive reward from the environment). So, the sooner the agent reaches the goal state, the quicker the  $\Gamma(t)$ , i.e., risk converges to zero. All the update rules defined in the paper can be derived from the postulate that the agent tries to minimise the (variational) free energy w.r.t the generative model [65, 76].



# 2 Extended Data

Fig. B1 DishBrain software schematics. a) Software components and data flow in the DishBrain closed loop system. Voltage samples flow from the MEA to the 'Pong' environment, and sensory information flows from the 'Pong' environment back to the MEA, forming a closed loop. The blue rectangles mark proprietary pieces of hardware from MaxWell, including the MEA well which may contain a live culture of neurons. The green MXWServer is a piece of software provided by MaxWell which is used to configure the MEA and Hub, using a private API directly over the network. The red rectangles mark components of the 'Dish-Server' program, a high-performance program consisting of four components designed to run asynchronously, despite being run on a single CPU thread. The 'LAN Interface' component stores the network state, for talking to the Hub, and produces arrays of voltage values for processing. Voltage values are passed to the 'Spike Detection' component, which stores feedback values and spike counts, and passes recalibration commands back to the LAN Interface. When the pong environment is ready to run, it updates the state of the paddle based on the spike counts, updates the state of the ball based on its velocity and collision conditions, and re-configures the stimulation sequencer based on the relative position of the ball and current state of the game. The stimulation sequencer stores and updates indices and countdowns relating to the stimulations it must produce and converts these into commands each time the corresponding countdown reaches zero, which are finally passed back to the LAN Interface, to send to the MEA system, closing the loop. The procedures associated with each component are run one after the other in a simple loop control flow, but the 'Pong' environment only moves forward every 200th update, short-circuiting otherwise. Additionally, up to three worker processes are launched in parallel, depending on which parts of the system need to be recorded. They receive data from the main thread via shared memory and write it to file, allowing the main thread to continue processing data without having to hand control to the operating system and back again. b) Numeric operations in the real-time spike detection component of the DishBrain closed loop system, including multiple IIR filters. Running a virtual environment in a closed loop imposes strict performance requirements, and digital signal processing is the main bottleneck of this system, with close to 42 MB of data to process every second. Simple sequences of IIR digital filters are applied to incoming data, storing multiple arrays of 1024 feedback values in between each sample. First, spikes on the incoming data are detected by applying a high pass filter to determine the deviation of the activity and comparing that to the MAD, which is itself calculated with a subsequent low pass filter. Then, a low pass filter is applied to the original data to determine whether the MEA hardware needs to be re-calibrated, affecting future samples. This system was able to keep up with the incoming data on a single thread of an Intel Core i7-8809G. Figures adapted from [6].



Fig. B2 Hyper-parameter exploration of RL algorithms. The changes in average hits-per-rally for each RL algorithm in several sample points of the grid search space. a) Effects of changing the learning rate on DQN performance. replay buffer size = 10000 and batch size = 32; b) Effects of changing the replay buffer size on DQN performance. learning rate = 0.0001 and batch size = 32; c) Effects of changing the batch size on DQN performance. learning rate = 0.0001 and replay buffer size = 10000; d) Effects of changing the actor learning rate = 0.0001 and replay buffer size = 10000; d) Effects of changing the actor learning rate on A2C performance. critic learning rate = 0.001 and batch size = 32; e) Effects of changing the batch size on A2C performance. actor learning rate = 0.0001 and batch size = 32; f) Effects of changing the batch size on A2C performance. actor learning rate = 0.0001 and critic learning rate = 0.001; g) Effects of changing the actor learning rate on PPO performance. critic learning rate = 0.001 and batch size = 32; h) Effects of changing the batch size on 22; h) Effects of changing rate = 0.001 and batch size = 32; h) Effects of changing rate = 0.001 and batch size = 32; i) Effects of changing rate = 0.001 and batch size = 32; i) Effects of changing rate = 0.001 and batch size = 32; i) Effects of changing rate = 0.001 and batch size = 32; i) Effects of changing the batch size on PPO performance. actor learning rate = 0.0001 and batch size = 32; i) Effects of changing the batch size on PPO performance. actor learning rate = 0.0001 and batch size = 32; i) Effects of changing the batch size on PPO performance. actor learning rate = 0.0001 and batch size = 32; i) Effects of changing the batch size on PPO performance. actor learning rate = 0.0001 and batch size = 32; i) Effects of changing the batch size on PPO performance. actor learning rate = 0.0001 and critic learning rate = 0.001.



Fig. B3 Image Input to DQN - Effects of changing the batch size. The Average number of a) hits-per-rally, b) % of aces, and c) % of long rallies over 20 minutes real-time equivalent of training DQN with batch sizes 8, 16, 32, 64, compared to the MCC and HCC cultures. d) average rally length over time, e) Average % of aces within groups and over time. f) Average % of long-rallies ( $\geq$  3) performed in a session. g,h and i) Pairwise Tukey's post-hoc test. Box plots show interquartile range, with bars demonstrating 1.5X interquartile range, the line marks the median and the black triangle marks the mean. Error bands = 1 SE.



Fig. B4 Image Input to A2C - Effects of changing the batch size. The Average number of a) hits-per-rally, b) % of aces, and c) % of long rallies over 20 minutes real-time equivalent of training A2C with batch sizes 8, 16, 32, 64, compared to the MCC and HCC cultures. d) average rally length over time, e) Average % of aces within groups and over time. f) Average % of long-rallies ( $\geq$  3) performed in a session. g,h and i) Pairwise Tukey's post-hoc test. Box plots show interquartile range, with bars demonstrating 1.5X interquartile range, the line marks the median and the black triangle marks the mean. Error bands = 1 SE.



Fig. B5 Image Input to PPO - Effects of changing the batch size. The Average number of a) hits-per-rally, b) % of aces, and c) % of long rallies over 20 minutes real-time equivalent of training PPO with batch sizes 8, 16, 32, 64, compared to the MCC and HCC cultures. d) average rally length over time, e) Average % of aces within groups and over time. f) Average % of long-rallies ( $\geq$  3) performed in a session. g,h and i) Pairwise Tukey's post-hoc test. Box plots show interquartile range, with bars demonstrating 1.5X interquartile range, the line marks the median and the black triangle marks the mean. Error bands = 1 SE.



Fig. B6 Relative improvement over time for various batch sizes of the RL algorithms. Relative improvement (%) in the average hit counts between the first 5 minutes and the last 15 minutes of all sessions as well as the post-hoc tests in each separate group for batch sizes of 8, 16, 32, and 64 in the a) DQN, b) A2C, and c) PPO groups compared to biological cultures.



Fig. B7 Extended training episodes for the deep RL algorithms. Training the implemented deep RL algorithms for 11000 game episodes using the same set of hyperparameters as in the main paper illustrates the increasing trend in their performance and high levels of total reward (i.e. episode duration) achieved. The plots show a moving average of the total episode reward with a window size of 100.



Fig. B8 Additional hidden layers in the DQN algorithm. BALL POSITION INPUT to the RL Algorithms: The average number of a) hits-per-rally, b) % of aces, and c) % of long rallies over 20 minutes real-time equivalent of training DQN (2 additional hidden layers, batch size = 32), A2C, PPO, and MCC, HCC cultures. d) average rally length over time, e) Average % of aces within groups and over time. f) Average % of long-rallies ( $\geq$  3) performed in a session. g,h and i) Pairwise Tukey's post-hoc test. PADDLE&BALL POSITION INPUT to the RL Algorithms: The average number of j) hits-per-rally, k) % of aces, and l) % of long rallies over 20 minutes real-time equivalent of training DQN (2 additional hidden layers, batch size = 32), A2C, PPO, and MCC, HCC cultures. m) average rally length over time, n) Average % of aces within groups and over time. o) Average % of long-rallies ( $\geq$  3) performed in a session. p,q and r) Pairwise Tukey's post hoc test. Box plots show interquartile range, with bars demonstrating 1.5X interquartile range, the line marks the median and the black triangle marks the mean. Error bands = 1 SE.



Fig. B9 Relative improvement over time with additional hidden layers in DQN algorithm. Relative improvement (%) in the average hit counts between the first 5 minutes and the last 15 minutes of all sessions in each separate group for a) BALL POSITION INPUT design for DQN with 2 additional hidden layers, b) PADDLE&BALL POSITION INPUT design for DQN with 2 additional hidden layers.



**Fig. B10** A schematic illustration of the overall network construction framework. The spiking time series data are first transformed into a 3D space using t-SNE embedding. These lower-dimensional representations are then combined into a tensor, which is decomposed using Tucker decomposition. The K-medoids algorithm is then applied to identify consistent representative channels across all cultures. These channels become network nodes, and pairwise Pearson correlation values serve as edge weights. The network layout reflects the physical placement of channels on the MEA, with node colors distinguishing sensory (green) from motor (blue) regions.



Fig. B11 Comparing Active Inference agent with biological neurons. a) Average rally length over time where this within-group increase was significant for all groups except CL(3) (One-way ANOVA test, p = 5.854e-6, p = 7.936-17, p = 0.873, and p = 2.254e-6, for MCC, HCC, CL(3), and CL(7) respectively). b) Average % of aces within groups and over time where this within-group increase was significant only for HCC, MCC, and CL(7) groups (One-way ANOVA test, p = 0.014, p = 2.907e-08, p = 0.380, and p = 0.016, for MCC, HCC, CL(3), and CL(7) respectively). c) Average % of long-rallies ( $\geq 3$ ) performed in a session where the increase over time was significant for all groups except CL(3) (One-way ANOVA test, p = 1.525e-24, p = 0.253, and p = 8.944e-4 for MCC, HCC, CL(3), and CL(7), respectively). d Relative improvement (%) in the average hit counts between the first 5 minutes and the last 15 minutes of all sessions in each separate group. e,f,g and h) Pairwise post hoc tests. Box plots show interquartile range, with bars demonstrating 1.5X interquartile range, the line marks the median and the black triangle marks the mean. Error bands = 1 SE.

Figure	Pan	Parameters	Sourc	Α	В	Mean	Mean	diff	se	Т	p-val	hedge	Method
1	el g	Hit Counts	e 0-5	A2C	DQN	(A) 0.705	0.709	-0.004	0.027	-0.147	0.900	-0.008	Tukey's
•	Б		Minute	A2C	HCC	0.705	0.651	0.055	0.025	2.151	0.199	0.110	
				A2C	MCC	0.705	0.716	-0.011	0.029	-0.373	0.900	-0.021	
				A2C	РРО	0.705	0.716	-0.011	0.029	-0.388	0.900	-0.022	
				DQN	HCC	0.709	0.651	0.059	0.025	2.310	0.142	0.117	
				DQN	MCC	0.709	0.716	-0.007	0.029	-0.237	0.900	-0.014	
				DQN	PPO	0.709	0.716	-0.007	0.029	-0.251	0.900	-0.014	
				HCC	MCC	0.651	0.716	-0.065	0.027	-2.386	0.120	-0.131	
				HCC	PPO	0.651	0.716	-0.066	0.027	-2.410	0.113	-0.132	
				MCC	PPO	0.716	0.716	-0.000	0.030	-0.013	0.900	-0.001	
			6-20	A2C	DQN	0.738	0.738	0.000	0.018	0.004	0.900	0.000	
			Minute	A2C	HCC	0.738	0.854	-0.117	0.017	-6.726	0.001	-0.198	
				A2C	MCC	0.738	0.852	-0.115	0.020	-5.715	0.001	-0.194	
				A2C	PPO	0.738	0.709	0.029	0.019	1.506	0.551	0.049	
				DQN	HCC	0.738	0.854	-0.117	0.017	-6.737	0.001	-0.198	
				DQN	MCC	0.738	0.852	-0.115	0.020	-5.723	0.001	-0.194	
				DQN	РРО	0.738	0.709	0.029	0.019	1.503	0.552	0.049	
				HCC	MCC	0.854	0.852	0.002	0.020	0.101	0.900	0.003	
				HCC	РРО	0.854	0.709	0.146	0.019	7.818	0.001	0.246	
				MCC	PPO	0.852	0.709	0.144	0.021	6.778	0.001	0.243	
	h	% Aces	0-5	A2C	DQN	51.842	52.190	-0.347	1.425	-0.244	0.900	-0.028	Tukey's
			s	A2C	HCC	51.842	54.382	-2.539	1.375	-1.847	0.348	-0.205	
				A2C	MCC	51.842	53.333	-1.490	1.549	-0.962	0.859	-0.120	
				A2C	PPO	51.842	54.731	-2.889	1.425	-2.028	0.254	-0.234	
				DQN	HCC	52.190	54.382	-2.192	1.375	-1.595	0.501	-0.177	
				DQN	MCC	52.190	53.333	-1.143	1.549	-0.738	0.900	-0.092	
				DQN	PPO	52.190	54.731	-2.542	1.425	-1.784	0.385	-0.205	
				HCC	MCC	54.382	53.333	1.049	1.503	0.698	0.900	0.085	
				HCC	PPO	54.382	54.731	-0.350	1.375	-0.254	0.900	-0.028	
				MCC	PPO	53.333	54.731	-1.399	1.549	-0.903	0.893	-0.113	
			6-20 Minuto	A2C	DQN	50.284	50.136	0.148	0.946	0.157	0.900	0.018	
			s	A2C	HCC	50.284	49.259	1.025	0.912	1.123	0.768	0.125	
				A2C	MCC	50.284	50.232	0.052	1.028	0.051	0.900	0.006	
				A2C	PPO	50.284	53.254	-2.970	0.946	-3.141	0.015	-0.362	
				DQN	HCC	50.136	49.259	0.877	0.912	0.961	0.860	0.107	
				DQN	MCC	50.136	50.232	-0.096	1.028	-0.093	0.900	-0.012	
				DQN	PPO	50.136	53.254	-3.118	0.946	-3.298	0.009	-0.380	
				HCC	MCC	49.259	50.232	-0.973	0.998	-0.975	0.852	-0.118	
				HCC	PPO	49.259	53.254	-3.995	0.912	-4.378	0.001	-0.487	
				MCC	PPO	50.232	53.254	-3.022	1.028	-2.940	0.028	-0.368	

 Table S2. Follow up main and supplementary text post-hoc tests for multivariate tests, including means, standard error (SE), t-scores, degree of freedom and exact p-values with hedges.

	i	% Long Rally	0-5 Minute	A2C	DQN	7.421	9.789	-2.368	0.913	-2.594	0.073	-0.299	Tukey's
			s	A2C	HCC	7.421	4.523	2.898	0.881	3.290	0.009	0.366	
				A2C	MCC	7.421	7.318	0.103	0.993	0.103	0.900	0.013	
				A2C	PPO	7.421	8.122	-0.701	0.913	-0.767	0.900	-0.088	
				DQN	HCC	9.789	4.523	5.267	0.881	5.978	0.001	0.665	
				DQN	MCC	9.789	7.318	2.471	0.993	2.489	0.094	0.312	
				DQN	PPO	9.789	8.122	1.667	0.913	1.826	0.360	0.210	
				HCC	MCC	4.523	7.318	-2.796	0.963	-2.903	0.031	-0.353	
				HCC	PPO	4.523	8.122	-3.599	0.881	-4.085	0.001	-0.454	
				MCC	PPO	7.318	8.122	-0.803	0.993	-0.809	0.900	-0.101	
			6-20	A2C	DQN	10.034	10.248	-0.214	0.623	-0.344	0.900	-0.040	
			Minute	A2C	HCC	10.034	10.365	-0.331	0.601	-0.550	0.900	-0.061	
			5	A2C	MCC	10.034	11.972	-1.938	0.677	-2.863	0.035	-0.358	
				A2C	PPO	10.034	8.506	1.528	0.623	2.454	0.102	0.283	
				DQN	HCC	10.248	10.365	-0.116	0.601	-0.194	0.900	-0.022	
				DQN	MCC	10.248	11.972	-1.724	0.677	-2.547	0.082	-0.319	
				DQN	PPO	10.248	8.506	1.743	0.623	2.798	0.042	0.322	
				HCC	MCC	10.365	11.972	-1.608	0.657	-2.447	0.104	-0.297	
				HCC	PPO	10.365	8.506	1.859	0.601	3.094	0.017	0.344	
				MCC	PPO	11.972	8.506	3.467	0.677	5.121	0.001	0.641	
2	σ	Hit Counts	0-5	A2C	DQN	0.722	0.713	0.009	0.027	0.325	0.900	0.017	Tukey's
_	0		Minute	A2C	HCC	0.722	0.651	0.072	0.026	2.761	0.046	0.141	
			s	A2C	MCC	0.722	0.716	0.006	0.029	0.216	0.900	0.012	
				A2C	PPO	0.722	0 740	-0.018	0.027	-0.641	0.900	-0.035	
				DON	HCC	0.713	0.651	0.063	0.026	2.428	0.108	0.123	
				DON	MCC	0.713	0.716	-0.003	0.029	-0.087	0.900	-0.005	
				DON	PPO	0.713	0.740	-0.026	0.027	-0.968	0.856	-0.052	
				HCC	MCC	0.651	0.716	-0.065	0.028	-2 335	0.134	-0.128	
				HCC	PPO	0.651	0.740	-0.089	0.026	-3 428	0.006	-0.175	
				MCC	PPO	0.716	0.740	-0.024	0.029	-0.815	0.900	-0.047	
					_	0.,10	0.710	0.02	0.02)	0.010	0.900	0.017	
			6-20	A2C	DQN	0.724	0.716	0.008	0.018	0.415	0.900	0.013	
			Minute s	A2C	HCC	0.724	0.854	-0.131	0.018	-7.461	0.001	-0.220	
				A2C	MCC	0.724	0.852	-0.129	0.020	-6.354	0.001	-0.216	
				A2C	PPO	0.724	0.727	-0.004	0.018	-0.217	0.900	-0.007	
				DQN	HCC	0.716	0.854	-0.138	0.017	-7.918	0.001	-0.232	
				DQN	MCC	0.716	0.852	-0.136	0.020	-6.743	0.001	-0.229	
				DQN	PPO	0.716	0.727	-0.011	0.018	-0.633	0.900	-0.019	
				HCC	MCC	0.854	0.852	0.002	0.020	0.100	0.900	0.003	
				HCC	PPO	0.854	0.727	0.127	0.018	7.233	0.001	0.213	
				MCC	PPO	0.852	0.727	0.125	0.020	6.158	0.001	0.210	
	h	% Aces	0-5	A2C	DQN	51.318	54.016	-2.698	1.469	-1.837	0.354	-0.212	Tukey's
			Minute s	A2C	HCC	51.318	54.382	-3.064	1.417	-2.162	0.196	-0.240	
			-	A2C	MCC	51.318	53.333	-2.014	1.597	-1.262	0.690	-0.158	
				A2C	PPO	51.318	50.866	0.453	1.469	0.308	0.900	0.035	
				DQN	HCC	54.016	54.382	-0.366	1.417	-0.258	0.900	-0.029	
				DQN	MCC	54.016	53.333	0.683	1.597	0.428	0.900	0.054	

				DQN	PPO	54.016	50.866	3.150	1.469	2.145	0.202	0.247	
				HCC	MCC	54.382	53.333	1.049	1.550	0.677	0.900	0.082	
				HCC	PPO	54.382	50.866	3.516	1.417	2.481	0.096	0.276	
				MCC	PPO	53.333	50.866	2.467	1.597	1.545	0.529	0.193	
			6-20	A2C	DQN	52.596	53.001	-0.404	0.919	-0.440	0.900	-0.051	
			Minute	A2C	HCC	52.596	49.259	3.337	0.887	3.762	0.002	0.418	
			-	A2C	MCC	52.596	50.232	2.364	0.999	2.366	0.126	0.296	
				A2C	PPO	52.596	51.658	0.938	0.919	1.020	0.826	0.118	
				DQN	HCC	53.001	49.259	3.741	0.887	4.218	0.001	0.469	
				DQN	MCC	53.001	50.232	2.769	0.999	2.771	0.045	0.347	
				DQN	PPO	53.001	51.658	1.342	0.919	1.460	0.577	0.168	
				HCC	MCC	49.259	50.232	-0.973	0.970	-1.003	0.836	-0.122	
				HCC	PPO	49.259	51.658	-2.399	0.887	-2.705	0.054	-0.301	
				MCC	PPO	50.232	51.658	-1.427	0.999	-1.428	0.595	-0.179	
	i	% Long Rally	0-5 Minuto	A2C	DQN	9.519	10.105	-0.586	0.990	-0.591	0.900	-0.068	Tukey's
			s	A2C	HCC	9.519	4.523	4.997	0.955	5.230	0.001	0.581	Tukey 5
				A2C	MCC	9.519	7.318	2.201	1.076	2.045	0.246	0.256	
				A2C	PPO	9.519	10.462	-0.942	0.990	-0.952	0.865	-0.110	
				DQN	HCC	10.105	4.523	5.582	0.955	5.843	0.001	0.650	
				DQN	MCC	10.105	7.318	2.787	1.076	2.589	0.074	0.324	
				DQN	PPO	10.105	10.462	-0.357	0.990	-0.360	0.900	-0.042	
				HCC	MCC	4.523	7.318	-2.796	1.044	-2.677	0.059	-0.325	
				HCC	PPO	4.523	10.462	-5.939	0.955	-6.217	0.001	-0.691	
				MCC	PPO	7.318	10.462	-3.144	1.076	-2.921	0.030	-0.366	
			6-20	A2C	DQN	10.431	11.238	-0.807	0.616	-1.311	0.661	-0.151	
			Minute	A2C	HCC	10.431	10.365	0.066	0.594	0.111	0.900	0.012	
				A2C	MCC	10.431	11.972	-1.541	0.669	-2.303	0.145	-0.288	
				A2C	PPO	10.431	10.049	0.382	0.616	0.620	0.900	0.071	
				DQN	HCC	11.238	10.365	0.873	0.594	1.470	0.571	0.163	
				DQN	MCC	11.238	11.972	-0.734	0.669	-1.097	0.783	-0.137	
				DQN	PPO	11.238	10.049	1.189	0.616	1.931	0.302	0.222	
				HCC	MCC	10.365	11.972	-1.608	0.649	-2.475	0.097	-0.301	
				HCC	PPO	10.365	10.049	0.316	0.594	0.531	0.900	0.059	
				MCC	PPO	11.972	10.049	1.923	0.669	2.873	0.034	0.360	
3	g	Hit Counts	0-5	A2C	DQN	0.771	0.687	0.084	0.028	2.980	0.024	0.159	Tukey's
	0		Minute	A2C	HCC	0.771	0.651	0.121	0.027	4.507	0.001	0.229	
			3	A2C	MCC	0.771	0.716	0.055	0.030	1.826	0.359	0.105	
				A2C	PPO	0.771	0.698	0.073	0.028	2.593	0.072	0.139	
				DQN	HCC	0.687	0.651	0.037	0.027	1.371	0.628	0.070	
				DQN	MCC	0.687	0.716	-0.029	0.030	-0.951	0.866	-0.055	
				DQN	PPO	0.687	0.698	-0.011	0.028	-0.375	0.900	-0.020	
			_	HCC	MCC	0.651	0 716	-0.065	0.029	-2.262	0.158	-0.124	
				HCC	PPO	0.651	0 698	-0.047	0.027	-1.759	0.399	-0.090	
				MCC	PPO	0.716	0.698	0.018	0.030	0 598	0.900	0.034	
			6-20			0.777	0.687	0.010	0.018	4 982	0.001	0.150	
			Minute	A2C	DQN	0.777	0.007	0.070	0.010	1.902	0.001	0.150	
			S	A2C	HCC	0.777	0.854	-0.077	0.018	-4.348	0.001	-0.128	

			A2C	MCC	0 777	0.952	0.075	0.020	2662	0.002	0.125	
			A2C	PPO	0.777	0.832	-0.075	0.020	-5.002	0.002	0.123	
			DON	HCC	0.687	0.854	-0.167	0.018	-9 521	0.003	-0.278	
			DON	MCC	0.687	0.852	-0.165	0.010	-9.321	0.001	-0.275	
			DON	PPO	0.687	0.712	-0.025	0.018	-1 389	0.617	-0.042	
			HCC	MCC	0.854	0.852	0.002	0.020	0.099	0.900	0.003	
			HCC	PPO	0.854	0.032	0.142	0.018	8 044	0.001	0.005	
			MCC	PPO	0.852	0.712	0.140	0.020	6 854	0.001	0.230	
h	% Aces	0-5	A2C	DON	53 293	55 443	-2.150	1 473	-1 459	0.577	-0.168	Tukey's
	,	Minute	A2C	HCC	53 293	54 382	-1 089	1 422	-0.766	0.900	-0.085	
		s	A2C	MCC	53 293	53 333	-0.040	1.602	-0.025	0.900	-0.003	
			A2C	PPO	53 293	54 248	-0.956	1 473	-0.649	0.900	-0.075	
			DON	HCC	55 443	54 382	1.061	1 422	0.746	0.900	0.073	
			DON	MCC	55 443	53 333	2 110	1.602	1 317	0.658	0.165	
			DON	PPO	55.443	54.248	1 194	1.002	0.811	0.900	0.093	
			HCC	MCC	54 382	53 333	1.174	1.554	0.675	0.900	0.093	
			НСС	PPO	54 382	54.248	0.133	1.331	0.094	0.900	0.002	
			MCC	PPO	53 333	54 248	-0.916	1.422	-0.572	0.900	-0.072	
		6-20	A2C	DON	52 530	53 870	1 3/10	0.966	1 307	0.500	0.161	
		Minute	A2C	HCC	52,530	10 250	3 270	0.900	3 508	0.013	0.300	
		s	A2C	MCC	52,530	50 232	2 208	1.050	2 188	0.185	0.390	
			A2C	PPO	52,530	52 511	0.018	0.066	2.100	0.185	0.274	
			DON	нсс	52.550	40.250	4.620	0.900	4.055	0.900	0.002	
			DON	MCC	52.970	49.239	4.020	1.050	4.933	0.001	0.331	
			DQN	PRO	52.079	52 511	1 269	0.066	3.472	0.003	0.455	
			DQN	MCC	33.879	50.222	1.308	0.900	1.413	0.002	0.105	
			нее	PRO	49.259	50.232	-0.973	0.022	-0.954	0.864	-0.116	
			MCC	PPO	49.239	52.511	-3.232	0.932	-3.488	0.003	-0.388	
			MCC	PPO	50.232	52.511	-2.280	1.050	-2.170	0.192	-0.272	
i	% Long Rally	0-5	A2C	DQN	9.810	9.334	0.236	0.935	0.274	0.900	0.032	Tukey's
1		Minute	A2C	HCC	9.810	4.523	5.288	0.902	5.861	0.001	0.652	
		5	A2C	MCC	9.810	7.318	2.492	1.016	2.452	0.103	0.307	
			A2C	PPO	9.810	9.403	0.408	0.935	0.436	0.900	0.050	
			DQN	HCC	9.554	4.523	5.032	0.902	5.577	0.001	0.620	
			DQN	MCC	9.554	7.318	2.236	1.016	2.200	0.181	0.275	
			DQN	PPO	9.554	9.403	0.151	0.935	0.162	0.900	0.019	
			HCC	MCC	4.523	7.318	-2.796	0.986	-2.834	0.038	-0.344	
			HCC	PPO	4.523	9.403	-4.880	0.902	-5.410	0.001	-0.601	
			MCC	PPO	7.318	9.403	-2.085	1.016	-2.051	0.243	-0.257	
		6-20 Minute	A2C	DQN	12.722	9.511	3.211	0.632	5.083	0.001	0.585	
	6-2 Min s	s	A2C	HCC	12.722	10.365	2.357	0.610	3.868	0.001	0.430	
			A2C	MCC	12.722	11.972	0.750	0.687	1.092	0.786	0.137	
			A2C	PPO	12.722	10.183	2.540	0.632	4.020	0.001	0.463	
			DQN	HCC	9.511	10.365	-0.854	0.610	-1.401	0.611	-0.156	
			DQN	MCC	9.511	11.972	-2.461	0.687	-3.584	0.003	-0.449	
			DQN	PPO	9.511	10.183	-0.672	0.632	-1.063	0.802	-0.122	
			HCC	MCC	10.365	11.972	-1.608	0.666	-2.412	0.113	-0.293	

			HCC	PPO	10.365	10.183	0.182	0.610	0.299	0.900	0.033	
			MCC	PPO	11.972	10.183	1.790	0.687	2.606	0.070	0.326	-
4	a	Average Paddle	A2C	DQN	71606.1 54	75257.4 36	3651.	4997. 725	-0.731	0.900	-0.164	Tukey's
		Movement	A2C	HCC	71606.1	52000.4 27	282 19605 727	3783.	5.182	0.001	0.886	
			A2C	MCC	71606.1 54	50007.5 04	21598	4190. 720	5.154	0.001	0.973	
			A2C	PPO	71606.1 54	72712.5 00	- 1106. 346	4966. 391	-0.223	0.900	-0.050	
			DQN	HCC	75257.4 36	52000.4 27	23257 .009	3783. 228	6.147	0.001	1.051	-
			DQN	MCC	75257.4 36	50007.5 04	25249 .932	4190. 720	6.025	0.001	1.138	
			DQN	PPO	75257.4 36	72712.5 00	2544. 936	4966. 391	0.512	0.900	0.114	
			НСС	MCC	52000.4 27	50007.5 04	1992. 923	2626. 345	0.759	0.900	0.090	
			НСС	PPO	52000.4 27	72712.5 00	20712 .073	3741. 737	-5.535	0.001	-0.936	
			MCC	PPO	50007.5 04	72712.5 00	- 22704 .996	4153. 302	-5.467	0.001	-1.023	
	b	Relative improvement	A2C	DQN	29.919	24.634	5.285	7.934	288.9 57	0.900	0.077	Games Howell
		(%) in the average hit counts	A2C	HCC	29.919	82.147	52.22 7	9.623	316.9 74	0.001	-0.603	
			A2C	MCC	29.919	50.755	20.83	9.830	223.4 64	0.215	-0.265	
			A2C	PPO	29.919	21.602	8.318	7.665	279.0 06	0.789	0.125	
			DQN	HCC	24.634	82.147	- 57.51 2	9.026	296.9 59	0.001	-0.708	
			DQN	MCC	24.634	50.755	26.12	9.246	197.1 21	0.041	-0.354	
			DQN	PPO	24.634	21.602	3.033	6.900	295.7 06	0.900	0.051	
			HCC	MCC	82.147	50.755	31.39 1	10.73 1	262.9 94	0.030	0.355	
			НСС	РРО	82.147	21.602	60.54 5	8.791	284.2 14	0.001	0.766	
			MCC	PPO	50.755	21.602	29.15 4	9.016	184.9 40	0.012	0.405	
	c	Average Paddle Movement	A2C	DQN	78719.2 50	83859.0 00	5139. 750	4264. 838	-1.205	0.722	-0.267	Tukey's
			A2C	HCC	78719.2 50	52000.4 27	26718 823	3233. 710	8.263	0.001	1.397	
			A2C	MCC	78719.2 50	50007.5 04	28711 .746	3589. 396	7.999	0.001	1.497	
			A2C	PPO	78719.2 50	75665.5 00	3053. 750	4264. 838	0.716	0.900	0.159	
			DQN	HCC	83859.0 00	52000.4 27	31858 .573	3233. 710	9.852	0.001	1.666	
			DQN	MCC	83859.0 00	50007.5 04	33851 .496	3589. 396	9.431	0.001	1.765	
			DQN	PPO	83859.0 00	75665.5 00	8193. 500	4264. 838	1.921	0.307	0.425	
			HCC	MCC	52000.4 27	50007.5 04	1992. 923	2269. 758	0.878	0.900	0.104	

		HCC	РРО	52000.4 27	75665.5 00	23665	3233. 710	-7.318	0.001	-1.238	
		MCC	PPO	50007.5 04	75665.5 00	- 25657 996	3589. 396	-7.148	0.001	-1.338	
d	Relative improvement (%) in the	A2C	DQN	21.717	36.623		10.28	245.4 47	0.584	-0.167	Games Howell
	average hit counts- Paddle&Ball Position Input	A2C	HCC	21.717	82.147	- 60.42 9	9.165	303.1 51	0.001	-0.733	
	r	A2C	MCC	21.717	50.755	29.03 8	9.381	203.8 60	0.019	-0.387	
		A2C	PPO	21.717	14.690	7.027	7.082	292.7 73	0.842	0.114	
		DQN	HCC	36.623	82.147	45.52	11.53 1	304.5 65	0.001	-0.439	
		DQN	MCC	36.623	50.755	14.13	11.70 3	257.8 34	0.720	-0.151	
		DQN	PPO	36.623	14.690	21.93	9.955	226.5 46	0.182	0.254	
		HCC	MCC	82.147	50.755	31.39	10.73	262.9 94	0.030	0.355	
		HCC	PPO	82.147	14.690	67.45	8.792	284.2	0.001	0.853	
		MCC	РРО	50.755	14.690	36.06	9.017	184.9 81	0.001	0.501	
e	Average Paddle Movement	A2C	DQN	67718.7 50	75019.2 50	- 7300. 500	4333. 263	-1.685	0.446	-0.373	Tukey's
		A2C	HCC	67718.7 50	52000.4 27	15718	3285. 592	4.784	0.001	0.809	
		A2C	MCC	67718.7 50	50007.5 04	17711 246	3646. 984	4.856	0.001	0.909	
		A2C	PPO	67718.7 50	73952.2 50	6233. 500	4333. 263	-1.439	0.589	-0.319	
		DQN	HCC	75019.2 50	52000.4 27	23018	3285. 592	7.006	0.001	1.185	
		DQN	MCC	75019.2	50007.5 04	25011 746	3646. 984	6.858	0.001	1.283	
		DQN	РРО	75019.2	73952.2	1067.	4333.	0.246	0.900	0.055	
		HCC	MCC	52000.4 27	50007.5 04	1992. 923	2306. 174	0.864	0.900	0.103	
		НСС	PPO	52000.4 27	73952.2 50	21951 .823	3285. 592	-6.681	0.001	-1.130	
		MCC	PPO	50007.5 04	73952.2 50	- 23944 .746	3646. 984	-6.566	0.001	-1.229	
f	Relative improvement	A2C	DQN	33.724	29.397	4.327	9.789	297.5 13	0.900	0.051	Games Howell
	(%) in the average hit counts- Ball	A2C	HCC	33.724	82.147	48.42	10.07 7	321.8 71	0.001	-0.534	
	Poisuon input	A2C	MCC	33.724	50.755	17.03	10.27 4	238.3 11	0.464	-0.207	
		A2C	PPO	33.724	33.016	0.709	10.30	292.7 92	0.900	0.008	
		DQN	НСС	29.397	82.147	52.74 9	10.26	321.8	0.001	-0.571	

				DQN	MCC	29.397	50.755	21.35	10.46 1	243.1 72	0.249	-0.256	
				DQN	РРО	29.397	33.016	-3.618	10.48	295.4	0.900	-0.040	-
				HCC	MCC	82.147	50.755	31.39	7 10.73	23 262.9	0.030	0.355	-
				HCC	PPO	82 147	33.016	1 49.13	10.75	94 317.8	0.001	0 508	-
				MCC	PPO	50 755	22.016	17.74	6	517.6	0.001	0.202	-
		W. O.		Denvis	PPO	30.755	33.016	0	10.94	252.1	0.486	0.203	
B3	g	Hit Counts	0-5 Minute	DQN_16	DQN_32	0.560	0.562	-0.002	0.045	-0.054	0.900	-0.005	Tukey's
			s	DON 16	DON 9	0.560	0.632	-0.072	0.046	-1.567	0.604	-0.150	-
				DQN_10	HCC	0.560	0.582	-0.022	0.040	-0.472	0.900	-0.043	-
				DON 16	MCC	0.560	0.051	-0.091	0.037	-2.437	0.137	-0.190	-
				DON 32	DON 64	0.562	0.632	-0.069	0.037	-1.566	0.605	-0.145	-
				DQN_32	DQN_8	0.562	0.582	-0.019	0.045	-0.433	0.005	-0.040	-
				DQN_32	HCC	0.562	0.651	-0.088	0.035	-2.522	0.118	-0.184	
				DQN_32	MCC	0.562	0.716	-0.154	0.037	-4.127	0.001	-0.321	-
				DQN_64	DQN_8	0.632	0.582	0.050	0.045	1.111	0.867	0.105	-
				DON (4	1100	0.(22	0.651	0.010	0.02(	0.525	0.000	0.020	-
				DQN_64	HCC	0.632	0.651	-0.019	0.036	-0.525	0.900	-0.039	
				DQN_64	MCC	0.632	0.716	-0.084	0.038	-2.220	0.229	-0.176	
				DQN_8	HCC	0.582	0.651	-0.069	0.036	-1.916	0.394	-0.144	-
				DQN_8	MCC	0.582	0.716	-0.134	0.038	-3.521	0.006	-0.281	
				HCC	MCC	0.651	0.716	-0.065	0.026	-2.490	0.127	-0.137	-
			6-20 Minute	DQN_16	DQN_32	0.567	0.560	0.007	0.031	0.232	0.900	0.012	
			s	DQN_16	DQN_64	0.567	0.634	-0.067	0.030	-2.207	0.235	-0.116	
				DQN_16	DQN_8	0.567	0.526	0.041	0.031	1.326	0.743	0.070	
				DQN_16	HCC	0.567	0.854	-0.288	0.025	11.61	0.001	-0.495	
				DQN_16	MCC	0.567	0.852	-0.286	0.027	- 10.70	0.001	-0.492	-
				DQN_32	DQN_64	0.560	0.634	-0.074	0.030	-2.442	0.142	-0.128	
				DQN_32	DQN_8	0.560	0.526	0.034	0.031	1.093	0.878	0.058	-
				DQN_32	HCC	0.560	0.854	-0.295	0.025	- 11.90	0.001	-0.508	-
				DQN_32	MCC	0.560	0.852	-0.293	0.027	6 - 10 97	0.001	-0.504	
				DQN_64	DQN_8	0.634	0.526	0.108	0.030	3,555	0.005	0.186	
				DQN_64	HCC	0.634	0.854	-0.220	0.024	-9.087	0.001	-0.380	
				DQN_64	MCC	0.634	0.852	-0.218	0.026	-8.335	0.001	-0.376	-

			DQN_8	HCC	0.526	0.854	-0.328	0.025	-	0.001	-0.566	
									13.30			
			DQN_8	MCC	0.526	0.852	-0.326	0.027	-	0.001	-0.562	
									12.27			
			HCC	MCC	0.854	0.852	0.002	0.019	0.103	0.900	0.003	
h	% Aces	0-5 Minute	DQN_16	DQN_32	53.103	58.358	-5.255	2.638	-1.992	0.349	-0.395	Tukey's
		s	DQN_16	DQN_64	53.103	54.163	-1.061	2.638	-0.402	0.900	-0.080	
			DQN_16	DQN_8	53.103	56.084	-2.981	2.638	-1.130	0.856	-0.224	
			DQN_16	HCC	53.103	54.382	-1.279	2.117	-0.604	0.900	-0.097	
			DQN_16	MCC	53.103	53.333	-0.230	2.250	-0.102	0.900	-0.017	
			DQN_32	DQN_64	58.358	54.163	4.194	2.638	1.590	0.591	0.316	
			DQN_32	DQN_8	58.358	56.084	2.274	2.638	0.862	0.900	0.171	
			DQN_32	HCC	58.358	54.382	3.976	2.117	1.879	0.419	0.300	
			DQN_32	MCC	58.358	53.333	5.025	2.250	2.234	0.224	0.379	
			DQN_64	DQN_8	54.163	56.084	-1.921	2.638	-0.728	0.900	-0.145	
			DQN_64	HCC	54.163	54.382	-0.219	2.117	-0.103	0.900	-0.017	
			DQN_64	MCC	54.163	53.333	0.831	2.250	0.369	0.900	0.063	
			DQN_8	HCC	56.084	54.382	1.702	2.117	0.804	0.900	0.129	
			DQN_8	MCC	56.084	53.333	2.751	2.250	1.223	0.802	0.208	
			HCC	MCC	54.382	53.333	1.049	1.607	0.653	0.900	0.079	
		6-20 Minute	DQN_16	DQN_32	56.069	55.545	0.524	1.744	0.300	0.900	0.060	
		s	DQN_16	DQN_64	56.069	55.105	0.964	1.744	0.553	0.900	0.110	
			DQN_16	DQN_8	56.069	59.565	-3.496	1.744	-2.004	0.341	-0.398	
			DQN_16	HCC	56.069	49.259	6.810	1.399	4.866	0.001	0.778	
			DQN_16	MCC	56.069	50.232	5.837	1.488	3.924	0.001	0.666	
			DQN_32	DQN_64	55.545	55.105	0.440	1.744	0.252	0.900	0.050	
			DQN_32	DQN_8	55.545	59.565	-4.020	1.744	-2.305	0.194	-0.457	
			DQN_32	HCC	55.545	49.259	6.286	1.399	4.491	0.001	0.718	
			DQN_32	MCC	55.545	50.232	5.313	1.488	3.572	0.005	0.606	
			DQN_64	DQN_8	55.105	59.565	-4.460	1.744	-2.557	0.110	-0.507	
			DQN_64	HCC	55.105	49.259	5.846	1.399	4.177	0.001	0.668	
			DQN_64	MCC	55.105	50.232	4.873	1.488	3.276	0.014	0.556	
			DONO			10.5-5				0.000		
			DQN_8	HCC	59.565	49.259	10.30 6	1.399	7.364	0.001	1.178	
			DQN 8	MCC	59 565	50 232	9 334	1 488	6 274	0.001	1.065	
					57.505	50.232	7.554	1.700	0.277	0.001	1.005	

				HCC	MCC	49.259	50.232	-0.973	1.062	-0.915	0.900	-0.111	
	i	% Long Rally	0-5 Minute	DQN_16	DQN_32	7.882	4.460	3.422	1.409	2.428	0.148	0.482	Tukey's
			s	DQN_16	DQN_64	7.882	7.083	0.798	1.409	0.567	0.900	0.112	
				DQN_16	DQN_8	7.882	6.948	0.933	1.409	0.662	0.900	0.131	
				DQN_16	HCC	7.882	4.523	3.359	1.130	2.972	0.037	0.475	
				DQN_16	MCC	7.882	7.318	0.563	1.202	0.469	0.900	0.080	
				DQN_32	DQN_64	4.460	7.083	-2.623	1.409	-1.862	0.429	-0.370	
				DQN_32	DQN_8	4.460	6.948	-2.488	1.409	-1.766	0.489	-0.350	
				DQN_32	HCC	4.460	4.523	-0.063	1.130	-0.055	0.900	-0.009	
				DQN_32	MCC	4.460	7.318	-2.858	1.202	-2.379	0.166	-0.404	
				DQN_64	DQN_8	7.083	6.948	0.135	1.409	0.096	0.900	0.019	
				DQN_64	HCC	7.083	4.523	2.561	1.130	2.265	0.210	0.362	
				DQN_64	MCC	7.083	7.318	-0.235	1.202	-0.195	0.900	-0.033	
				DQN_8	HCC	6.948	4.523	2.426	1.130	2.146	0.266	0.343	
				DQN_8	MCC	6.948	7.318	-0.370	1.202	-0.308	0.900	-0.052	
				HCC	MCC	4.523	7.318	-2.796	0.858	-3.258	0.015	-0.396	
			6-20 Minute	DQN_16	DQN_32	6.138	6.310	-0.172	0.929	-0.185	0.900	-0.037	
			s	DQN_16	DQN_64	6.138	6.916	-0.777	0.929	-0.837	0.900	-0.166	
				DQN_16	DQN_8	6.138	6.221	-0.083	0.929	-0.089	0.900	-0.018	
				DQN_16	HCC	6.138	10.365	-4.226	0.746	-5.668	0.001	-0.906	
				DQN_16	MCC	6.138	11.972	-5.834	0.793	-7.361	0.001	-1.250	
				DQN_32	DQN_64	6.310	6.916	-0.605	0.929	-0.651	0.900	-0.129	
				DQN_32	DQN_8	6.310	6.221	0.090	0.929	0.096	0.900	0.019	
				DQN_32	HCC	6.310	10.365	-4.054	0.746	-5.438	0.001	-0.870	
				DQN_32	MCC	6.310	11.972	-5.662	0.793	-7.144	0.001	-1.213	
				DQN_64	DQN_8	6.916	6.221	0.695	0.929	0.748	0.900	0.148	
				DQN_64	HCC	6.916	10.365	-3.449	0.746	-4.626	0.001	-0.740	
				DQN_64	MCC	6.916	11.972	-5.057	0.793	-6.380	0.001	-1.083	
				DQN_8	HCC	6.221	10.365	-4.144	0.746	-5.558	0.001	-0.889	
				DQN_8	MCC	6.221	11.972	-5.751	0.793	-7.257	0.001	-1.232	
B4	g	Hit Counts	0-5 Minute	A2C_16	A2C_32	0.629	0.730	-0.101	0.044	-2.308	0.191	-0.214	Tukey's
			s	A2C_16	A2C_64	0.629	0.638	-0.009	0.044	-0.208	0.900	-0.019	
				A2C_16	A2C_8	0.629	0.655	-0.026	0.044	-0.594	0.900	-0.056	
				A2C_16	HCC	0.629	0.651	-0.021	0.035	-0.611	0.900	-0.045	
				A2C_16	MCC	0.629	0.716	-0.087	0.037	-2.326	0.184	-0.184	
				A2C_32	A2C_64	0.730	0.638	0.092	0.043	2.115	0.280	0.195	
				A2C_32	A2C_8	0.730	0.655	0.075	0.044	1.710	0.521	0.158	
				A2C_32	HCC	0.730	0.651	0.080	0.035	2.302	0.193	0.169	
				A2C_32	MCC	0.730	0.716	0.014	0.037	0.386	0.900	0.030	

### Springer Nature 2021 LATEX template

				A2C_64	A2C_8	0.638	0.655	-0.017	0.044	-0.390	0.900	-0.036	
				A2C_64	HCC	0.638	0.651	-0.012	0.035	-0.355	0.900	-0.026	-
				A2C_64	MCC	0.638	0.716	-0.078	0.037	-2.104	0.286	-0.165	-
				A2C_8	НСС	0.655	0.651	0.005	0.035	0.136	0.900	0.010	
				A2C_8	MCC	0.655	0.716	-0.061	0.037	-1.626	0.570	-0.128	-
				нсс	MCC	0.651	0.716	-0.065	0.026	-2.523	0.118	-0.139	
			6-20 Minute	A2C_16	A2C_32	0.605	0.705	-0.100	0.031	-3.254	0.015	-0.173	-
			s	A2C_16	A2C_64	0.605	0.622	-0.017	0.031	-0.541	0.900	-0.029	-
				A2C_16	A2C_8	0.605	0.597	0.008	0.031	0.256	0.900	0.014	-
				A2C_16	HCC	0.605	0.854	-0.250	0.025	-9.962	0.001	-0.430	-
				A2C_16	MCC	0.605	0.852	-0.248	0.027	-9.188	0.001	-0.426	-
				A2C_32	A2C_64	0.705	0.622	0.083	0.031	2.735	0.069	0.144	-
				A2C_32	A2C_8	0.705	0.597	0.108	0.031	3.526	0.006	0.186	-
				A2C_32	HCC	0.705	0.854	-0.149	0.024	-6.122	0.001	-0.257	-
				A2C_32	MCC	0.705	0.852	-0.147	0.026	-5.595	0.001	-0.254	-
				A2C_64	A2C_8	0.622	0.597	0.025	0.031	0.801	0.900	0.043	-
				A2C_64	HCC	0.622	0.854	-0.233	0.025	-9.427	0.001	-0.401	-
				A2C_64	MCC	0.622	0.852	-0.231	0.027	-8.673	0.001	-0.397	
				A2C_8	HCC	0.597	0.854	-0.258	0.025	10.33	0.001	-0.444	
				A2C_8	MCC	0.597	0.852	-0.256	0.027	-9.531	0.001	-0.440	-
				НСС	MCC	0.854	0.852	0.002	0.019	0.103	0.900	0.003	-
	h	% Aces	0-5	A2C_16	A2C_32	53.810	54.083	-0.272	2.370	-0.115	0.900	-0.023	Tukey's
			Minute s	A2C_16	A2C_64	53.810	53.299	0.511	2.370	0.216	0.900	0.043	-
				A2C_16	A2C_8	53.810	52.332	1.478	2.370	0.624	0.900	0.124	-
				A2C_16	HCC	53.810	54.382	-0.571	1.901	-0.301	0.900	-0.048	-
				A2C_16	MCC	53.810	53.333	0.478	2.021	0.236	0.900	0.040	-
				A2C_32	A2C_64	54.083	53.299	0.783	2.370	0.331	0.900	0.066	-
				A2C_32	A2C_8	54.083	52.332	1.750	2.370	0.738	0.900	0.147	
				A2C_32	HCC	54.083	54.382	-0.299	1.901	-0.157	0.900	-0.025	
				A2C_32	MCC	54.083	53.333	0.750	2.021	0.371	0.900	0.063	-
				A2C_64	A2C_8	53.299	52.332	0.967	2.370	0.408	0.900	0.081	-
				A2C_64	HCC	53.299	54.382	-1.083	1.901	-0.569	0.900	-0.091	
				A2C_64	MCC	53.299	53.333	-0.034	2.021	-0.017	0.900	-0.003	-
l					1								

			A2C_8	HCC	52.332	54.382	-2.049	1.901	-1.078	0.886	-0.172	
			A2C_8	MCC	52.332	53.333	-1.000	2.021	-0.495	0.900	-0.084	
			HCC	MCC	54.382	53.333	1.049	1.443	0.727	0.900	0.088	
		6-20 Minuto	A2C_16	A2C_32	53.076	52.170	0.906	1.627	0.557	0.900	0.110	
		s	A2C_16	A2C_64	53.076	52.981	0.094	1.627	0.058	0.900	0.012	
			A2C_16	A2C_8	53.076	54.117	-1.042	1.627	-0.640	0.900	-0.127	
			A2C_16	HCC	53.076	49.259	3.816	1.305	2.924	0.042	0.468	
			A2C_16	MCC	53.076	50.232	2.844	1.388	2.049	0.316	0.348	
			A2C_32	A2C_64	52.170	52.981	-0.811	1.627	-0.499	0.900	-0.099	
			A2C_32	A2C_8	52.170	54.117	-1.947	1.627	-1.197	0.817	-0.238	
			A2C_32	HCC	52.170	49.259	2.911	1.305	2.230	0.226	0.357	
			A2C_32	MCC	52.170	50.232	1.938	1.388	1.397	0.702	0.237	
			A2C_64	A2C_8	52.981	54.117	-1.136	1.627	-0.698	0.900	-0.139	
			A2C_64	HCC	52.981	49.259	3.722	1.305	2.851	0.051	0.456	
			A2C_64	MCC	52.981	50.232	2.749	1.388	1.981	0.355	0.336	
			A2C_8	HCC	54.117	49.259	4.858	1.305	3.721	0.003	0.595	
			A2C_8	MCC	54.117	50.232	3.885	1.388	2.800	0.059	0.475	
			HCC	MCC	49.259	50.232	-0.973	0.991	-0.981	0.900	-0.119	
i	% Long Rally	0-5	A2C_16	A2C_32	5.395	6.147	-0.752	1.314	-0.572	0.900	-0.114	Tukey's
		Minute s	A2C_16	A2C_64	5.395	6.973	-1.578	1.314	-1.201	0.815	-0.238	
			A2C_16	A2C_8	5.395	5.357	0.038	1.314	0.029	0.900	0.006	
			A2C_16	HCC	5.395	4.523	0.872	1.054	0.828	0.900	0.132	
			A2C_16	MCC	5.395	7.318	-1.923	1.120	-1.717	0.518	-0.291	
			A2C_32	A2C_64	6.147	6.973	-0.826	1.314	-0.629	0.900	-0.125	
			A2C_32	A2C_8	6.147	5.357	0.790	1.314	0.602	0.900	0.119	
			A2C_32	HCC	6.147	4.523	1.624	1.054	1.541	0.619	0.246	
			A2C_32	MCC	6.147	7.318	-1.171	1.120	-1.045	0.900	-0.177	
			A2C_64	A2C_8	6.973	5.357	1.617	1.314	1.231	0.798	0.244	
			A2C_64	HCC	6.973	4.523	2.451	1.054	2.325	0.186	0.372	
			A2C_64	MCC	6.973	7.318	-0.345	1.120	-0.308	0.900	-0.052	
			A2C 8	HCC	5 357	4 523	0.834	1 054	0 791	0.900	0.127	
					5.557	1.525	0.051	1.001	0.791	0.900	0.127	
			A2C_8	MCC	5.357	7.318	-1.962	1.120	-1.751	0.498	-0.297	
			НСС	MCC	4.523	7.318	-2.796	0.800	-3.494	0.007	-0.424	
		6-20 Minute	A2C_16	A2C_32	6.077	7.705	-1.628	0.942	-1.727	0.512	-0.343	
		s	A2C_16	A2C_64	6.077	6.942	-0.865	0.942	-0.917	0.900	-0.182	

-			1				1		I	1	1	1	1
				A2C_16	A2C_8	6.077	6.231	-0.154	0.942	-0.163	0.900	-0.032	
				A2C_16	HCC	6.077	10.365	-4.287	0.756	-5.671	0.001	-0.907	
				A2C_16	MCC	6.077	11.972	-5.895	0.804	-7.336	0.001	-1.245	
				A2C_32	A2C_64	7.705	6.942	0.763	0.942	0.810	0.900	0.161	-
				A2C_32	A2C_8	7.705	6.231	1.474	0.942	1.564	0.606	0.310	-
				A2C_32	HCC	7.705	10.365	-2.660	0.756	-3.518	0.006	-0.563	-
				A2C_32	MCC	7.705	11.972	-4.267	0.804	-5.310	0.001	-0.901	-
				A2C_64	A2C_8	6.942	6.231	0.711	0.942	0.754	0.900	0.150	-
				A2C_64	HCC	6.942	10.365	-3.423	0.756	-4.528	0.001	-0.724	-
				A2C_64	MCC	6.942	11.972	-5.030	0.804	-6.260	0.001	-1.063	-
				A2C_8	HCC	6.231	10.365	-4.134	0.756	-5.468	0.001	-0.874	-
				A2C_8	MCC	6.231	11.972	-5.741	0.804	-7.144	0.001	-1.213	-
				HCC	MCC	10.365	11.972	-1.608	0.574	-2.801	0.059	-0.340	-
B5	g	Hit Counts	0-5 Minute	<i>PPO_</i> 16	PP0_32	0.557	0.555	0.002	0.044	0.035	0.900	0.003	Tukey's
			s	<i>PPO_</i> 16	PP0_64	0.557	0.632	-0.075	0.044	-1.684	0.537	-0.159	-
				PP0_16	PPO_8	0.557	0.552	0.005	0.045	0.121	0.900	0.011	-
				<i>PPO_</i> 16	HCC	0.557	0.651	-0.094	0.035	-2.639	0.088	-0.199	-
				<i>PPO_</i> 16	MCC	0.557	0.716	-0.159	0.038	-4.227	0.001	-0.338	-
				PP0_32	<i>PPO_</i> 64	0.555	0.632	-0.076	0.044	-1.734	0.508	-0.162	-
				<i>PPO_</i> 32	<i>PPO_</i> 64	0.555	0.552	0.004	0.044	0.088	0.900	0.008	-
				PP0_32	HCC	0.555	0.651	-0.095	0.035	-2.720	0.072	-0.202	-
				<i>PPO_</i> 32	MCC	0.555	0.716	-0.161	0.037	-4.322	0.001	-0.341	-
				<i>PPO_</i> 64	PPO_8	0.632	0.552	0.080	0.044	1.816	0.457	0.171	-
				<i>PPO</i> _64	HCC	0.632	0.651	-0.019	0.035	-0.536	0.900	-0.040	
				PPO 64	MCC	0.632	0.716	-0.084	0.037	-2 262	0.210	-0.179	-
						0.002	0.710	0.001	0.007	2.202	0.210	0.175	
				PPO_8	HCC	0.552	0.651	-0.099	0.035	-2.816	0.055	-0.211	-
				PPO_8	MCC	0.552	0.716	-0.164	0.037	-4.405	0.001	-0.350	
				1100	160	0.651	0.51.6	0.015	0.000			0.120	-
				псс	MCC	0.651	0.716	-0.065	0.026	-2.532	0.115	-0.139	
			6-20	PP0_16	PP0_32	0.508	0.523	-0.015	0.030	-0.486	0.900	-0.026	
			Minute s	PP0_16	PP0_64	0.508	0.513	-0.005	0.030	-0.160	0.900	-0.008	-
				PP0_16	PPO_8	0.508	0.556	-0.048	0.030	-1.579	0.597	-0.083	-
				PP0_16	HCC	0.508	0.854	-0.347	0.024	-	0.001	-0.607	-
										14.20			
				PP0_16	MCC	0.508	0.852	-0.345	0.026	-	0.001	-0.603	
										13.11			
				<i>PPO_</i> 32	<i>PPO</i> _64	0.523	0.513	0.010	0.030	0.328	0.900	0.017	

			PPO 32	PP0 64	0.523	0.556	-0.033	0.030	-1.090	0.880	-0.058	
			PP0 32	HCC	0.523	0.550	0.332	0.030	-1.090	0.001	0.581	
			110_02	nee	0.525	0.054	-0.552	0.024	13.61	0.001	-0.581	
			PP0_32	MCC	0.523	0.852	-0.330	0.026	-	0.001	-0.577	
			<b>BBO (4</b>	<b>BBO 0</b>	0.512	0.556	0.042	0.020	12.50	0.607	0.075	
			<i>PP0</i> _64	PP0_8	0.513	0.556	-0.043	0.030	-1.424	0.68/	-0.075	
			<i>PP0</i> _64	нсс	0.513	0.854	-0.342	0.024	14.09	0.001	-0.598	
			<i>PPO_</i> 64	MCC	0.513	0.852	-0.340	0.026	- 12.99	0.001	-0.595	
			PPO_8	HCC	0.556	0.854	-0.299	0.024	7	0.001	-0.523	
			<b>DDO</b> O	100	0.556	0.050	0.007	0.026	6	0.001	0.500	
			PP0_8	MCC	0.556	0.852	-0.297	0.026	11.42 2	0.001	-0.520	
			HCC	MCC	0.854	0.852	0.002	0.019	0.104	0.900	0.003	
h	% Aces	0-5 Minute	PP0_16	PP0_32	59.143	59.654	-0.511	2.553	-0.200	0.900	-0.040	Tukey's
		s	PP0_16	<i>PPO</i> _64	59.143	55.534	3.610	2.553	1.414	0.692	0.281	
			PP0_16	PPO_8	59.143	58.904	0.239	2.553	0.094	0.900	0.019	
			PP0_16	HCC	59.143	54.382	4.762	2.048	2.325	0.186	0.372	
			PP0_16	MCC	59.143	53.333	5.811	2.177	2.669	0.084	0.453	
			PP0_32	PP0_64	59.654	55.534	4.120	2.553	1.614	0.577	0.320	
			PP0_32	<i>PPO_</i> 64	59.654	58.904	0.750	2.553	0.294	0.900	0.058	
			PP0_32	HCC	59.654	54.382	5.273	2.048	2.575	0.106	0.412	
			PP0_32	MCC	59.654	53.333	6.322	2.177	2.904	0.044	0.493	
			PP0_64	PPO_8	55.534	58.904	-3.370	2.553	-1.320	0.746	-0.262	
			PP0_64	HCC	55.534	54.382	1.152	2.048	0.563	0.900	0.090	
			PP0_64	MCC	55.534	53.333	2.201	2.177	1.011	0.900	0.172	
			PPO_8	HCC	58.904	54.382	4.522	2.048	2.208	0.236	0.353	
			PPO_8	MCC	58.904	53.333	5.571	2.177	2.559	0.110	0.434	
			HCC	MCC	54.382	53.333	1.049	1.555	0.675	0.900	0.082	
		6-20 Minuto	PP0_16	PP0_32	60.504	60.595	-0.091	1.900	-0.048	0.900	-0.010	
		s	PP0_16	PP0_64	60.504	60.941	-0.438	1.900	-0.230	0.900	-0.046	
			PP0_16	PPO_8	60.504	58.316	2.187	1.900	1.151	0.844	0.228	
			PP0_16	HCC	60.504	49.259	11.24	1.524	7.376	0.001	1.180	
			<i>PPO_</i> 16	MCC	60.504	50.232	4 10.27 2	1.620	6.339	0.001	1.076	
			PP0_32	<i>PPO</i> _64	60.595	60.941	-0.347	1.900	-0.182	0.900	-0.036	
			PP0_32	PP0_64	60.595	58.316	2.279	1.900	1.199	0.816	0.238	
			PP0_32	HCC	60.595	49.259	11.33	1.524	7.436	0.001	1.189	
			PP0_32	MCC	60.595	50.232	10.36	1.620	6.395	0.001	1.086	

				PP0_64	PPO_8	60.941	58.316	2.625	1.900	1.382	0.711	0.274	
				<i>PPO_</i> 64	HCC	60.941	49.259	11.68	1.524	7.663	0.001	1.225	
				<i>PPO_</i> 64	MCC	60.941	50.232	10.70	1.620	6.609	0.001	1.122	-
				PPO_8	HCC	58.316	49.259	9.057	1.524	5.941	0.001	0.950	
				PPO_8	MCC	58.316	50.232	8.084	1.620	4.989	0.001	0.847	
			НСС	MCC	49.259	50.232	-0.973	1.157	-0.840	0.900	-0.102		
	i	% Long Rally	0-5	<i>PPO_</i> 16	PP0_32	4.885	5.501	-0.616	1.359	-0.453	0.900	-0.090	Tukey's
			Minute s	PP0_16	PP0_64	4.885	7.393	-2.508	1.359	-1.845	0.439	-0.366	-
				PP0_16	PPO_8	4.885	6.020	-1.135	1.359	-0.835	0.900	-0.166	-
				PP0_16	HCC	4.885	4.523	0.362	1.090	0.332	0.900	0.053	-
				PP0_16	MCC	4.885	7.318	-2.433	1.159	-2.099	0.290	-0.356	
				PP0_32	<i>PPO_</i> 64	5.501	7.393	-1.892	1.359	-1.392	0.705	-0.276	
				PP0_32	PP0_64	5.501	6.020	-0.519	1.359	-0.382	0.900	-0.076	076
				PP0_32	HCC	5.501	4.523	0.979	1.090	0.897	0.900	0.144	-
				PP0_32	MCC	5.501	7.318	-1.817	1.159	-1.568	0.604	-0.266	
				<i>PPO_</i> 64	PPO_8	7.393	6.020	1.373	1.359	1.010	0.900	0.201	-
				PP0_64	HCC	7.393	4.523	2.871	1.090	2.633	0.091	0.421	-
				PP0_64	MCC	7.393	7.318	0.075	1.159	0.065	0.900	0.011	
				PPO_8	HCC	6.020	4.523	1.497	1.090	1.373	0.716	0.220	-
				PPO_8	MCC	6.020	7.318	-1.298	1.159	-1.120	0.862	-0.190	-
				HCC	MCC	4.523	7.318	-2.796	0.828	-3.377	0.010	-0.410	-
			6-20 Minute	<i>PPO_</i> 16	PP0_32	6.008	5.224	0.784	0.871	0.900	0.900	0.179	
			s	<i>PPO_</i> 16	<i>PPO_</i> 64	6.008	5.339	0.669	0.871	0.769	0.900	0.153	
				PP0_16	PPO_8	6.008	6.234	-0.226	0.871	-0.260	0.900	-0.052	
				<i>PPO_</i> 16	HCC	6.008	10.365	-4.357	0.699	-6.237	0.001	-0.997	
				PP0_16	MCC	6.008	11.972	-5.964	0.743	-8.032	0.001	-1.363	
				PP0_32	<i>PPO_</i> 64	5.224	5.339	-0.114	0.871	-0.131	0.900	-0.026	
				PP0_32	<i>PPO_</i> 64	5.224	6.234	-1.010	0.871	-1.160	0.839	-0.230	
				PP0_32	HCC	5.224	10.365	-5.140	0.699	-7.358	0.001	-1.177	'7
				PP0_32	MCC	5.224	11.972	-6.748	0.743	-9.088	0.001	-1.543	
				PP0_64	PPO_8	5.339	6.234	-0.896	0.871	-1.029	0.900	-0.204	1
				PP0_64	HCC	5.339	10.365	-5.026	0.699	-7.195	0.001	-1.151	
				PP0_64	MCC	5.339	11.972	-6.634	0.743	-8.934	0.001	-1.517	1
		PP	PPO_8	HCC	6.234	10.365	-4.130	0.699	-5.913	0.001	-0.946		
				PPO_8	MCC	6.234	11.972	-5.738	0.743	-7.728	0.001	-1.312	

		1											1
				нсс	MCC	10.365	11.972	-1.608	0.530	-3.031	0.031	-0.368	
<b>B8</b>	g	Hit Counts	0-5 Minute	A2C	DQN	0.771	0.717	0.054	0.028	1.937	0.298	0.103	Tukey's
			s	A2C	HCC	0.771	0.651	0.121	0.027	4.508	0.001	0.229	-
				A2C	MCC	0.771	0.716	0.055	0.030	1.827	0.359	0.105	
				A2C	PPO	0.771	0.698	0.073	0.028	2.594	0.072	0.139	-
				DQN	HCC	0.717	0.651	0.066	0.027	2.476	0.096	0.126	_
				DQN	MCC	0.717	0.716	0.001	0.030	0.025	0.900	0.001	_
				DQN	PPO	0.717	0.698	0.019	0.028	0.668	0.900	0.036	_
				HCC	MCC	0.651	0.716	-0.065	0.029	-2.263	0.157	-0.124	_
				HCC	PPO	0.651	0.698	-0.047	0.027	-1.760	0.399	-0.090	_
				MCC	PPO	0.716	0.698	0.018	0.030	0.598	0.900	0.034	
			6-20 Minute	A2C	DQN	0.777	0.762	0.016	0.018	0.866	0.900	0.026	
			s	A2C	HCC	0.777	0.854	-0.077	0.018	-4.329	0.001	-0.127	-
				A2C	MCC	0.777	0.852	-0.075	0.021	-3.647	0.002	-0.124	-
				A2C	PPO	0.777	0.712	0.065	0.018	3.561	0.003	0.108	-
				DQN	HCC	0.762	0.854	-0.093	0.018	-5.262	0.001	-0.153	
				DQN	MCC	0.762	0.852	-0.091	0.020	-4.442	0.001	-0.150	-
				DQN	PPO	0.762	0.712	0.049	0.018	2.723	0.051	0.082	-
				HCC	MCC	0.854	0.852	0.002	0.020	0.099	0.900	0.003	-
				HCC	PPO	0.854	0.712	0.142	0.018	8.009	0.001	0.235	-
				MCC	PPO	0.852	0.712	0.140	0.021	6.825	0.001	0.232	-
	h	% Aces	0-5	A2C	DQN	53.293	52.579	0.714	1.455	0.491	0.900	0.057	Tukey's
			Minute	A2C	HCC	53.293	54.382	-1.089	1.404	-0.776	0.900	-0.086	-
			5	A2C	MCC	53.293	53.333	-0.040	1.582	-0.025	0.900	-0.003	-
				A2C	PPO	53.293	54.248	-0.956	1.455	-0.657	0.900	-0.076	-
				DQN	HCC	52.579	54.382	-1.803	1.404	-1.284	0.677	-0.143	-
				DQN	MCC	52.579	53.333	-0.754	1.582	-0.477	0.900	-0.060	-
				DQN	PPO	52.579	54.248	-1.670	1.455	-1.147	0.754	-0.132	-
				HCC	MCC	54.382	53.333	1.049	1.535	0.683	0.900	0.083	-
				HCC	PPO	54.382	54.248	0.133	1.404	0.095	0.900	0.011	-
				MCC	PPO	53.333	54.248	-0.916	1.582	-0.579	0.900	-0.072	-
			6-20	A2C	DQN	52.530	49.935	2.595	0.959	2.706	0.054	0.312	-
			Minute	A2C	HCC	52.530	49.259	3.270	0.925	3.535	0.004	0.393	-
			3	A2C	MCC	52.530	50.232	2.298	1.042	2.205	0.179	0.276	-
				A2C	PPO	52.530	52.511	0.018	0.959	0.019	0.900	0.002	-
				DQN	HCC	49.935	49.259	0.676	0.925	0.730	0.900	0.081	-
				DQN	MCC	49.935	50.232	-0.297	1.042	-0.285	0.900	-0.036	-
				DQN	PPO	49.935	52.511	-2.576	0.959	-2.687	0.057	-0.310	-
				HCC	MCC	49.259	50.232	-0.973	1.011	-0.962	0.860	-0.117	-
				HCC	PPO	49.259	52.511	-3.252	0.925	-3.515	0.004	-0.391	-
				MCC	PPO	50.232	52.511	-2.280	1.042	-2.187	0.186	-0.274	-
	i	% Long Rally	0-5	A2C	DON	12 722	10 195	2 527	0.631	4 004	0.001	0 461	Tukev's
	1		Minute	A2C	HCC	12 722	10 365	2.357	0.609	3 871	0.001	0.430	,
			s	A2C	MCC	12 722	11 972	0.750	0.686	1.093	0.785	0.137	-
						12.722	11.772	0.750	0.000	1.075	0.705	0.157	

				A2C	PPO	12.722	10.183	2.540	0.631	4.024	0.001	0.463	
				DQN	HCC	10.195	10.365	-0.169	0.609	-0.278	0.900	-0.031	
				DQN	MCC	10.195	11.972	-1.777	0.686	-2.590	0.073	-0.324	
				DQN	PPO	10.195	10.183	0.013	0.631	0.020	0.900	0.002	
				HCC	MCC	10.365	11.972	-1.608	0.666	-2.415	0.113	-0.293	
				HCC	PPO	10.365	10.183	0.182	0.609	0.299	0.900	0.033	
				MCC	PPO	11.972	10.183	1.790	0.686	2.609	0.070	0.327	
			6-20 Minute	A2C	DQN	11.266	9.629	1.637	0.589	2.777	0.044	0.226	
			s	A2C	HCC	11.266	7.444	3.823	0.569	6.721	0.001	0.529	
				A2C	MCC	11.266	9.645	1.621	0.641	2.530	0.085	0.224	
				A2C	РРО	11.266	9.793	1.474	0.589	2.500	0.091	0.204	
				DQN	нсс	9.629	7.444	2.186	0.569	3.843	0.001	0.302	02 02 123 105 125
				DQN	MCC	9.629	9.645	-0.016	0.641	-0.025	0.900	-0.002	
				DQN	РРО	9.629	9.793	-0.163	0.589	-0.277	0.900	-0.023	
				HCC	MCC	7.444	9.645	-2.202	0.622	-3.540	0.004	-0.305	
				HCC	PPO	7.444	9.793	-2.349	0.569	-4.130	0.001	-0.325	
DA		Uit Counts	0.5	MCC	PPO	9.645	9.793	-0.14/	0.641	-0.230	0.900	-0.020	Televerte
ВЭ	g	Hit Counts	0-5 Minute	A2C	DQN	0.722	0./19	0.003	0.027	0.124	0.900	0.007	Tukey s
			s	A2C	MCC	0.722	0.651	0.072	0.026	2.773	0.044	0.141	
				A2C	PPO	0.722	0.710	0.000	0.029	0.217	0.900	0.012	
			DON	HCC	0.722	0.740	-0.018	0.027	-0.044	0.900	-0.033		
			DON	MCC	0.719	0.051	0.003	0.020	0.101	0.002	0.155		
				DON	PPO	0.719	0.710	-0.021	0.029	-0.769	0.900	-0.041	
				HCC	MCC	0.719	0.740	-0.021	0.027	2 3 4 6	0.300	0.120	
				НСС	PPO	0.651	0.740	-0.005	0.026	-3.444	0.005	-0.125	
				MCC	PPO	0.051	0.740	-0.032	0.020	-0.819	0.005	-0.047	
						0.710	0.710	0.021	0.025	0.019	0.900	0.017	
			6-20	A2C	DON	0 724	0 741	-0.017	0.018	-0 947	0.868	-0.029	
			Minute	A2C	HCC	0.724	0.854	-0.131	0.017	-7 488	0.001	-0.220	9
			s	A2C	MCC	0.724	0.852	-0.129	0.020	-6.378	0.001	-0.217	
				A2C	PPO	0.724	0.727	-0.004	0.018	-0.218	0.900	-0.007	
				DQN	HCC	0.741	0.854	-0.114	0.017	-6.567	0.001	-0.192	
				DQN	MCC	0.741	0.852	-0.112	0.020	-5.570	0.001	-0.189	
				DQN	PPO	0.741	0.727	0.013	0.018	0.727	0.900	0.022	
				HCC	MCC	0.854	0.852	0.002	0.020	0.100	0.900	0.003	
				HCC	PPO	0.854	0.727	0.127	0.017	7.259	0.001	0.214	
				MCC	PPO	0.852	0.727	0.125	0.020	6.181	0.001	0.211	
	h	% Aces	0-5	A2C	DQN	51.318	53.675	-2.356	1.437	-1.640	0.473	-0.189	Tukey's
			Minute	A2C	HCC	51.318	54.382	-3.064	1.387	-2.209	0.177	-0.246	
			5	A2C	MCC	51.318	53.333	-2.014	1.562	-1.289	0.674	-0.161	
				A2C	PPO	51.318	50.866	0.453	1.437	0.315	0.900	0.036	
				DQN	HCC	53.675	54.382	-0.707	1.387	-0.510	0.900	-0.057	
				DQN	MCC	53.675	53.333	0.342	1.562	0.219	0.900	0.027	
				DQN	PPO	53.675	50.866	2.809	1.437	1.955	0.290	0.225	_
				HCC	MCC	54.382	53.333	1.049	1.516	0.692	0.900	0.084	
				HCC	PPO	54.382	50.866	3.516	1.387	2.536	0.084	0.282	

				MCC	PPO	53.333	50.866	2.467	1.562	1.579	0.510	0.198		
			6-20 Minute	A2C	DQN	52.596	51.199	1.397	0.907	1.540	0.532	0.177		
			s	A2C	HCC	52.596	49.259	3.337	0.875	3.813	0.001	0.424		
				A2C	MCC	52.596	50.232	2.364	0.986	2.398	0.117	0.300		
				A2C	PPO	52.596	51.658	0.938	0.907	1.034	0.818	0.119		
				DQN	HCC	51.199	49.259	1.940	0.875	2.217	0.175	0.246		
				DQN	MCC	51.199	50.232	0.968	0.986	0.981	0.848	0.123		
				DQN	PPO	51.199	51.658	-0.459	0.907	-0.506	0.900	-0.058		
				HCC	MCC	49.259	50.232	-0.973	0.957	-1.017	0.828	-0.124		
				HCC	PPO	49.259	51.658	-2.399	0.875	-2.742	0.049	-0.305		
				MCC	PPO	50.232	51.658	-1.427	0.986	-1.447	0.584	-0.181		
	i	% Long Rally	0-5	A2C	DQN	9.519	9.710	-0.191	0.965	-0.198	0.900	-0.023	Tukey's	
			Minute	A2C	HCC	9.519	4.523	4.997	0.931	5.366	0.001	0.596		
				A2C	MCC	9.519	7.318	2.201	1.049	2.098	0.222	0.263		
				A2C	PPO	9.519	10.462	-0.942	0.965	-0.976	0.851	-0.112		
				DQN	HCC	9.710	4.523	5.188	0.931	5.571	0.001	0.619		
				DQN	MCC	9.710	7.318	2.392	1.049	2.280	0.153	0.285		
					DQN	PPO	9.710	10.462	-0.752	0.965	-0.779	0.900	-0.090	
					HCC	MCC	4.523	7.318	-2.796	1.018	-2.746	0.048	-0.334	
				HCC	РРО	4.523	10.462	-5.939	0.931	-6.378	0.001	-0.709		
				MCC	PPO	7.318	10.462	-3.144	1.049	-2.996	0.024	-0.375		
			6-20	A2C	DQN	10.431	10.187	0.244	0.591	0.413	0.900	0.048		
			Minute	A2C	HCC	10.431	10.365	0.066	0.570	0.116	0.900	0.013		
				A2C	MCC	10.431	11.972	-1.541	0.642	-2.400	0.117	-0.300		
				A2C	PPO	10.431	10.049	0.382	0.591	0.646	0.900	0.074		
				DQN	HCC	10.187	10.365	-0.178	0.570	-0.312	0.900	-0.035		
				DQN	MCC	10.187	11.972	-1.785	0.642	-2.780	0.044	-0.348		
				DQN	PPO	10.187	10.049	0.138	0.591	0.233	0.900	0.027		
				HCC	MCC	10.365	11.972	-1.608	0.623	-2.579	0.075	-0.313		
				HCC	PPO	10.365	10.049	0.316	0.570	0.554	0.900	0.062		
				MCC	PPO	11.972	10.049	1.923	0.642	2.994	0.024	0.375		
B6	a	Relative improvement		DQN_16	DQN_32	6.400	43.207	36.80	17.55 4	75.73 3	0.300	-0.416	Games Howell	
		average hit		DQN_16	DQN_64	6.400	22.119	- 6	13.19	94.59	0.820	-0.236		
		counts – DQN			-			15.71 9	4	7				
				DQN_16	DQN_8	6.400	12.525	-6.124	12.50	97.07	0.900	-0.097		
				DQN_16	HCC	6.400	82.147	- 75.74	11.22 9	133.2 16	0.001	-1.079		
				DQN_16	MCC	6.400	50.755	6	11.40	126.2	0.002	-0.660		
			DOM 22	DONCA	42.207	22.110	44.35	18.47	60	0.040	0.222			
				DQN_32	DQN_64	43.207	22.119	21.08	18.47	84.89	0.848	0.227		
				DQN_32	DQN_8	43.207	12.525	30.68 2	17.98 3	80.30 0	0.527	0.339		
				DQN_32	HCC	43.207	82.147		17.12 2	73.46 2	0.218	-0.364		

			DQN_32	MCC	43.207	50.755	-7.549	17.23	74.55	0.900	-0.074	
			DQN_64	DQN_8	22.119	12.525	9.594	13.75 9	97.14 5	0.900	0.138	-
			DON 64	нсс	22 110	82 1 <i>47</i>		12.61	106.0	0.001	0.761	-
			DQ11_01	nee	22.119	82.147	60.02 7	4	83	0.001	-0.701	
			DQN_64	MCC	22.119	50.755	28.63	12.77 2	105.8 63	0.228	-0.381	-
			DQN_8	НСС	12.525	82.147	-	11.88	118.9	0.001	-0.936	-
							69.62 2	9	17			
			DQN_8	MCC	12.525	50.755	38.23 1	12.05 7	115.6 35	0.023	-0.538	
			НСС	MCC	82.147	50.755	31.39 1	10.73 1	262.9 94	0.043	0.355	-
	b	Relative improvement	A2C_16	A2C_32	18.203	23.304	-5.101	11.70	97.98 5	0.900	-0.087	Games Howell
		(%) in the average hit	A2C_16	A2C_64	18.203	23.700	-5.497	13.38 0	92.45 7	0.900	-0.082	-
		counts – A2C	A2C_16	A2C_8	18.203	13.710	4.493	10.92 9	96.32 5	0.900	0.082	
			A2C_16	HCC	18.203	82.147	- 63.94 4	11.09 8	136.5 51	0.001	-0.921	
			A2C_16	MCC	18.203	50.755	32.55	11.27 7	128.5 59	0.051	-0.490	-
			A2C_32	A2C_64	23.304	23.700	-0.396	13.44	92.95	0.900	-0.006	-
			A2C_32	A2C_8	23.304	13.710	9.594	11.00	96.00	0.900	0.173	-
			A2C_32	HCC	23.304	82.147	58.84	11.17 5	134.5 80	0.001	-0.842	-
			A2C_32	MCC	23.304	50.755	27.45	11.35 3	127.2 09	0.158	-0.410	
			A2C_64	A2C_8	23.700	13.710	9.990	12.77	86.48	0.900	0.155	-
			A2C_64	HCC	23.700	82.147	58.44	12.92 3	102.8 20	0.001	-0.723	-
			A2C_64	MCC	23.700	50.755	27.05	13.07 7	102.2 71	0.312	-0.351	
			A2C_8	HCC	13.710	82.147	68.43	10.36 4	158.7 02	0.001	-1.056	-
			A2C_8	MCC	13.710	50.755	37.04	10.55 6	142.0 25	0.008	-0.596	-
			HCC	MCC	82.147	50.755	31.39 1	10.73 1	262.9 94	0.043	0.355	-
	c	Relative improvement	PP0_16	PP0_32	24.036	11.686	12.35 0	14.07 7	81.19 4	0.900	0.174	Games Howell
		(%) in the average hit	PP0_16	<i>PPO</i> _64	24.036	-1.291	25.32 6	14.03 7	80.68 3	0.470	0.358	
		counto - r r O	PP0_16	PPO_8	24.036	49.866	25.83	25.19 0	75.51 6	0.900	-0.204	
			PP0_16	HCC	24.036	82.147	58.11	14.13 2	90.26 2	0.001	-0.658	
L		1		L	1		-					1

			PP0_16	MCC	24.036	50.755	26.72	14.27 4	90.89 8	0.428	-0.318								
			PP0_32	<i>PPO_</i> 64	11.686	-1.291	12.97 7	10.33 8	97.98 9	0.783	0.249								
			PP0_32	<i>PPO</i> _64	11.686	49.866	38.18	23.33 3	59.66 2	0.568	-0.325								
			PP0_32	НСС	11.686	82.147	70.46	10.46 8	155.1 89	0.001	-1.076								
			PP0_32	MCC	11.686	50.755	- 39.07 0	10.65 8	140.1 07	0.005	-0.622								
			<i>PPO_</i> 64	PPO_8	-1.291	49.866	51.15	23.30 8	59.44 5	0.256	-0.436								
		Relative	<i>PPO_</i> 64	HCC	-1.291	82.147	83.43	10.41 4	157.0 04	0.001	-1.281								
			<i>PP0_</i> 64	MCC	-1.291	50.755	52.04	10.60 5	141.1 09	0.001	-0.833								
			PPO_8	HCC	49.866	82.147	32.28	23.36 6	60.51 4	0.712	-0.221								
				PPO_8	MCC	49.866	50.755	-0.889	23.45 2	61.22 4	0.900	-0.006							
			HCC	MCC	82.147	50.755	31.39	10.73	262.9 94	0.043	0.355								
<b>B10</b> a	a	Relative improvement	A2C	DQN	33.724	28.251	5.473	8.669	283.8	0.900	0.073	Games Howell							
		average hit counts – Ball Position Input	A2C	нсс	33.724	82.147	48.42	10.07	321.8	0.001	-0.534								
			A2C	MCC	33.724	50.755	17.03	10.27 4	238.3 11	0.464	-0.207	•							
			A2C	РРО	33.724	33.016	0.709	10.30 1	292.7 92	0.900	0.008								
			DQN	HCC	28.251	82.147	53.89 6	9.206	304.7 84	0.001	-0.651								
			DQN	MCC	28.251	50.755	22.50	9.421	205.7 71	0.123	-0.299								
			DQN	РРО	28.251	33.016	-4.765	9.450	266.0 29	0.900	-0.058								
										НСС	MCC	82.147	50.755	31.39 1	10.73 1	262.9 94	0.030	0.355	
			НСС	РРО	82.147	33.016	49.13 1	10.75 6	317.8 52	0.001	0.508								
			MCC	PPO	50.755	33.016	17.74 0	10.94 1	252.1 47	0.486	0.203								
	b	Relative improvement	A2C	DQN	21.717	24.949	-3.232	8.194	291.1 51	0.900	-0.045	Games Howell							
		(%) in the average hit counts – Paddle&Ball	A2C	НСС	21.717	82.147	60.42 9	9.165	303.1 51	0.001	-0.733								
		counts – Paddle&Ball Position Input	Paddle&Ball Position Input	A2C	MCC	21.717	50.755	29.03	9.381	203.8 60	0.019	-0.387							
			A2C	РРО	21.717	14.690	7.027	7.082	292.7 73	0.842	0.114								
										DQN	HCC	24.949	82.147	57.19 7	9.711	318.5 26	0.001	-0.655	

				DQN	MCC	24.949	50.755	-	9.915	226.6	0.073	-0.326	
								25.80		15			
				DQN	PPO	24.949	14.690	10.25	7.775	276.1	0.657	0.152	
				HCC	MCC	82.147	50.755	31.39	10.73	262.9	0.030	0.355	
				HCC	PPO	82.147	14.690	67.45	8.792	284.2	0.001	0.853	-
				MCC	PPO	50.755	14.690	36.06	9.017	184.9 81	0.001	0.501	
5	e	Hit Counts	0-5	CL(3)	CL(7)	0.696	0.682	0.014	0.050	0.281	0.900	0.027	Tuckey's
			Minute	CL(3)	HCC	0.696	0.651	0.045	0.039	1.147	0.641	0.088	
				CL(3)	MCC	0.696	0.716	-0.020	0.042	-0.484	0.900	-0.039	-
				CL(7)	HCC	0.682	0.651	0.031	0.039	0.804	0.834	0.061	-
				CL(7)	MCC	0.682	0.716	-0.034	0.041	-0.827	0.821	-0.066	-
				HCC	MCC	0.651	0.716	-0.065	0.028	-2.318	0.094	-0.127	
			6-20	CL(3)	CL(7)	0.703	0.916	-0.213	0.039	-5.439	0.001	-0.336	
				Minute	CL(3)	HCC	0.703	0.854	-0.151	0.030	-4.972	0.001	-0.239
				CL(3)	MCC	0.703	0.852	-0.149	0.032	-4.624	0.001	-0.236	
				CL(7)	HCC	0.916	0.854	0.061	0.030	2.017	0.182	0.097	
				CL(7)	MCC	0.916	0.852	0.063	0.032	1.962	0.203	0.100	-
				HCC	MCC	0.854	0.852	0.002	0.021	0.094	0.900	0.003	-
	f	%Aces	0-5	CL(3)	CL(7)	53.140	54.239	-1.099	2.560	-0.429	0.900	-0.095	-
		Mis	Minute s	CL(3)	HCC	53.140	54.382	-1.242	2.008	-0.618	0.900	-0.108	
				CL(3)	MCC	53.140	53.333	-0.192	2.114	-0.091	0.900	-0.017	-
				CL(7)	HCC	54.239	54.382	-0.143	2.008	-0.071	0.900	-0.012	
				CL(7)	MCC	54.239	53.333	0.906	2.114	0.429	0.900	0.079	
				HCC	MCC	54.382	53.333	1.049	1.395	0.752	0.863	0.091	
			6-20	CL(3)	CL(7)	55.605	47.256	8.349	1.712	4.876	0.001	1.080	
			Minute	CL(3)	HCC	55.605	49.259	6.346	1.343	4.726	0.001	0.826	
				CL(3)	MCC	55.605	50.232	5.373	1.414	3.800	0.001	0.698	
				CL(7)	HCC	47.256	49.259	-2.003	1.343	-1.492	0.445	-0.261	
				CL(7)	MCC	47.256	50.232	-2.976	1.414	-2.105	0.154	-0.387	
				HCC	MCC	49.259	50.232	-0.973	0.933	-1.043	0.700	-0.127	
	g	%Long Rally	0-5	CL(3)	CL(7)	7.692	6.923	0.769	1.432	0.537	0.900	0.119	
			Minute	CL(3)	HCC	7.692	4.523	3.170	1.123	2.822	0.026	0.493	
				CL(3)	MCC	7.692	7.318	0.374	1.183	0.316	0.900	0.058	
				CL(7)	HCC	6.923	4.523	2.401	1.123	2.138	0.143	0.373	-
				CL(7)	MCC	6.923	7.318	-0.395	1.183	-0.334	0.900	-0.061	-
				HCC	MCC	4.523	7.318	-2.796	0.780	-3.583	0.002	-0.435	-
			6-20	CL(3)	CL(7)	9.292	12.160	-2.868	1.111	-2.582	0.050	-0.572	-
		6-20 Minute s	CL(3)	HCC	9.292	10.365	-1.073	0.871	-1.232	0.594	-0.215		
			CL(3)	MCC	9.292	11.972	-2.680	0.917	-2.923	0.019	-0.537		
			CL(7)	HCC	12.160	10.365	1.795	0.871	2.061	0.168	0.360		
				CL(7)	MCC	12.160	11.972	0.187	0.917	0.204	0.900	0.038	
				HCC	MCC	10.365	11.972	-1.608	0.605	-2.657	0.041	-0.323	
	h	Relative improvement (%) in the		CL(3)	CL(7)	20.341	54.109	33.76	15.95 3	-2.117	0.157	-0.469	Games Howell
average hit	CL(3)	HCC	20.341	82.147	-	14.02	-4.407	0.001	-0.770				
-------------	-------	-----	--------	--------	-------	-------	--------	-------	--------	--			
counts -	- (-)				61.80	3							
Active					6								
Inference	CL(3)	MCC	20.341	50.755	-	14.16	-2.147	0.148	-0.394				
					30.41	5							
					4								
	CL(7)	HCC	54.109	82.147	-	13.00	-2.157	0.144	-0.377				
					28.03	0							
					8								
	CL(7)	MCC	54.109	50.755	3.353	13.15	0.255	0.900	0.047				
						4							
	HCC	MCC	82.147	50.755	31.39	10.73	2.925	0.019	0.355				
					1	1							

Table S3. Multivariate statistical tests and all results for tests done.

Figure	Panel	Parameters	Source	DF1	DF2	MS	F	p-value	np2	Method
1	d	Average Rally	Group - all	4	729	0.185	1.021	0.395	0.006	
		Length	Time Interval - all	1	729	2.134	-21.944	1.000	-0.031	Mixed ANOVA
			Interaction - all	4	729	0.575	-5.909	1.000	-0.034	
	e	% Aces	Group - all	4	729	0.044	1.014	0.399	0.006	
			Time Interval - all	1	729	0.124	-5.589	1.000	-0.008	Mixed ANOVA
			Interaction - all	4	729	0.015	-0.685	1.000	-0.004	
	f	% Long Rally	Group - all	4	729	0.019	1.749	0.137	0.010	Mixed
			Time Interval - all	1	729	0.063	-11.125	1.000	-0.015	ANOVA
			Interaction - all	4	729	0.039	-6.931	1.000	-0.040	
2	d	Average Rally	Group - all	4	729	0.170	0.926	0.448	0.005	
		Length	Time Intervals - all	1	729	1.488	-15.161	1.000	-0.021	Mixed ANOVA
			Interaction - all	4	729	0.704	-7.170	1.000	-0.041	
	e	% Aces	Group - all	4	729	0.061	1.332	0.256	0.007	
			Time Intervals - all	1	729	0.022	-0.957	1.000	-0.001	ANOVA
			Interaction - all	4	729	0.041	-1.745	1.000	-0.010	
	f	% Long Rally	Group - all	4	729	0.011	0.886	0.472	0.005	Mixed
			Time Intervals - all	1	729	0.073	-11.249	1.000	-0.016	ANOVA
			Interaction - all	4	729	0.033	-5.038	1.000	-0.028	
3	d	Average Rally	Group - all	4	729	0.499	2.589	0.036	0.014	
		Length	Time Intervals- all	1	729	1.934	-18.645	1.000	-0.026	Mixed ANOVA
			Interaction - all	4	729	0.599	-5.774	1.000	-0.033	
	e	% Aces	Group - all	4	729	0.111	2.331	0.055	0.013	
			Time Intervals- all	1	729	0.111	-4.583	1.000	-0.006	Mixed ANOVA
			Interaction - all	4	729	0.021	-0.871	1.000	-0.005	
	f	% Long Rally	Group - all	4	729	0.018	1.523	0.194	0.008	Mixed
			Time Intervals - all	1	729	0.081	-12.847	1.000	-0.018	ANOVA
			Interaction - all	4	729	0.032	-5.057	1.000	-0.029	
B3	d		Group - all	5	478	1.645	8.293	0.0	0.080	

## Springer Nature 2021 $\ensuremath{\texttt{LATEX}}$ template

## 74 Biological Neurons vs Deep Reinforcement Learning

		Average Rally Length	Time Intervals	1	478	2.153	-18.414	1.0	-0.040	Mixed ANOVA	
			Interaction - all	5	478	0.443	-3.787	1.0	-0.041		
	e	% Aces	Group - all	5	478	0.259	5.194	0.0	0.052	Mixed	
			Time Intervals	1	478	0.059	-2.212	1.0	-0.005	ANOVA	
			Interaction - all	5	478	0.027	-1.008	1.0	-0.011		
	f	% Long Rally	Group - all	5	478	0.049	4.611	0.0	0.046	Mixed	
	1 /0 Long Kany		Time Intervals - all	1	478	0.113	-18.808	1.0	-0.041	ANOVA	
			Interaction - all	5	478	0.019	-3.197	1.0	-0.035		
B4	d	Average Rally	Group - all	5	478	0.765	4.206	0.001	0.042	Mixed	
		Length	Time Intervals - all	1	478	1.873	-17.980	1.000	-0.039	ANOVA	
			Interaction - all	5	478	0.502	-4.819	1.000	-0.053		
	e	% Aces	Group - all	5	478	0.060	1.410	0.219	0.015	Mixed	
			Time Intervals - all	1	478	0.050	-2.277	1.000	-0.005	ANOVA	
			Interaction - all	5	478	0.029	-1.306	1.000	-0.014		
	f	% Long Rally	Group - all	5	478	0.032	2.926	0.013	0.030	Mixed	
			Time Intervals - all	1	478	0.081	-13.550	1.000	-0.029	ANOVA	
			Interaction - all	5	478	0.026	-4.281	1.000	-0.047		
B5	d	Average Rally	Group - all	5	478	2.177	10.721	0.0	0.101	Mixed	
		Length	Time Intervals - all	1	478	1.503	-12.236	1.0	-0.026	ANOVA	
			Interaction - all	5	478	0.645	-5.254	1.0	-0.058		
	e	% Aces	Group - all	5	478	0.421	7.738	0.0	0.075	Mixed	
			Time Intervals - all	1	478	0.029	-0.970	1.0	-0.002	ANOVA	
			Interaction - all	5	478	0.046	-1.526	1.0	-0.016		
	f	% Long Rally	Group - all	5	478	0.046	4.651	0.0	0.046	Mixed	
			Time Intervals - all	1	478	0.095	-16.734	1.0	-0.036	ANOVA	
			Interaction - all	5	478	0.025	-4.406	1.0	-0.048		
<b>B8</b>	d	Average Rally	Group - all	4	729	0.260	1.372	0.242	0.007	Mixed	
		Length	Time Intervals - all	1	729	2.355	-23.160	1.000	-0.033	ANOVA	
			Interaction - all	4	729	0.525	-5.161	1.000	-0.029		
	e	% Aces	Group - all	4	729	0.066	1.445	0.217	0.008	Mixed	
			Time Intervals - all	1	729	0.141	-5.986	1.000	-0.008	ANOVA	
			Interaction - all	4	729	0.021	-0.897	1.000	-0.005		
	f	% Long Rally	Group - all	4	729	0.017	1.370	0.243	0.007	Mixed	
			Time Intervals - all	1	729	0.113	-17.552	1.000	-0.025	ANUVA	
			Interaction - all	4	729	0.024	-3.684	1.000	-0.021		
<b>B9</b>	d	Average Rally	Group - all	4	729	0.136	0.756	0.554	0.004	Mixed	
		Length	Time Intervals - all	1	729	1.690	-17.577	1.000	-0.025	ANUVA	
			Interaction - all	4	729	0.663	-6.889	1.000	-0.039		

	e	% Aces	Group - all	4	729	0.032	0.712	0.584	0.004	Mixed
			Time Intervals - all	1	729	0.054	-2.376	1.000	-0.003	ANOVA
			Interaction - all	4	729	0.042	-1.838	1.000	-0.010	
	f	% Long Rally	Group - all	4	729	0.009	0.763	0.55	0.004	Mixed
			Time Intervals - all	1	729	0.073	-11.682	1.00	-0.016	ANOVA
			Interaction - all	4	729	0.032	-5.152	1.00	-0.029	
5	a	Average Rally	Group - all	3	360	0.160	0.792	0.499	0.007	Mixed
		Length	Time Intervals - all	1	360	4.486	-38.506	1.000	-0.120	ANOVA
			Interaction - all	3	360	0.286	-2.454	1.000	-0.021	
	b	% Aces	Group - all	3	360	0.033	0.844	0.471	0.007	Mixed
			Time Intervals - all	1	360	0.162	-7.936	1.000	-0.023	ANOVA
			Interaction - all	3	360	0.031	-1.503	1.000	-0.013	
	c	% Long Rally	Group - all	3	360	0.012	1.004	0.391	0.008	Mixed
			Time Intervals - all	1	360	0.234	-36.162	1.000	-0.112	ANOVA
			Interaction - all	3	360	0.003	-0.517	1.000	-0.004	

Table S4. Multivariate statistical tests and all results for tests done.

Figure	Panel	Parameters	Source	DF	MS	F	p- value	np2	Method
4	а	Average Paddle Movement	Group - all	4	1.064e+10	21.837	0.0	0.155	ANOVA
	b	Relative improvement (%) in the average hit counts	Group - all	4	104528.369	17.807	0.0	0.089	ANOVA
	с	Average Paddle Movement	Group - all	4	1.801e+10	49.523	0.0	0.293	ANOVA
	d	Relative improvement (%) in the average hit counts	Group - all	4	116698.296	16.243	0.0	0.082	ANOVA
	e	Average Paddle Movement	Group - all	4	1.009e+10	26.881	0.0	0.184	ANOVA
	f	Relative improvement (%) in the average hit counts	Group - all	4	79671.720	9.889	0.0	0.051	ANOVA
5	d	Relative improvement (%) in the average hit counts – Active Inference	Group - all	3	52072.238	6.733	0.0	0.053	ANOVA
B6	a	Relative improvement (%) in the average hit counts - DQN	Group - all	5	77257.903	10.241	0.0	0.097	ANOVA
	b	Relative improvement (%) in the average hit counts – A2C	Group - all	5	73239.513	11.211	0.0	0.105	ANOVA

## Springer Nature 2021 $\text{LAT}_{EX}$ template

## 76 Biological Neurons vs Deep Reinforcement Learning

	c	Relative improvement (%) in the average hit counts - PPO	Group - all	5	83698.926	9.517	0.0	0.091	ANOVA
B10	a	Relative improvement (%) in the average hit counts - Ball Position Input	Group - all	4	81200.989	10.941	0.0	0.057	ANOVA
	b	Relative improvement (%) in the average hit counts - Paddle&Ball Position Input	Group - all	4	125476.158	20.915	0.0	0.103	ANOVA