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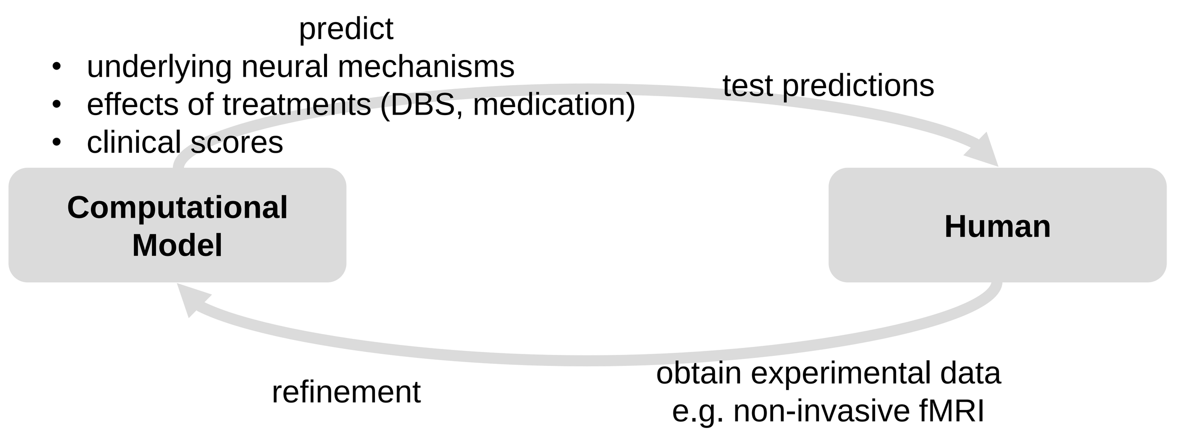
Professorship
Artificial Intelligence

# BOLD Monitoring in the Neural Simulator ANNarchy

## Motivation

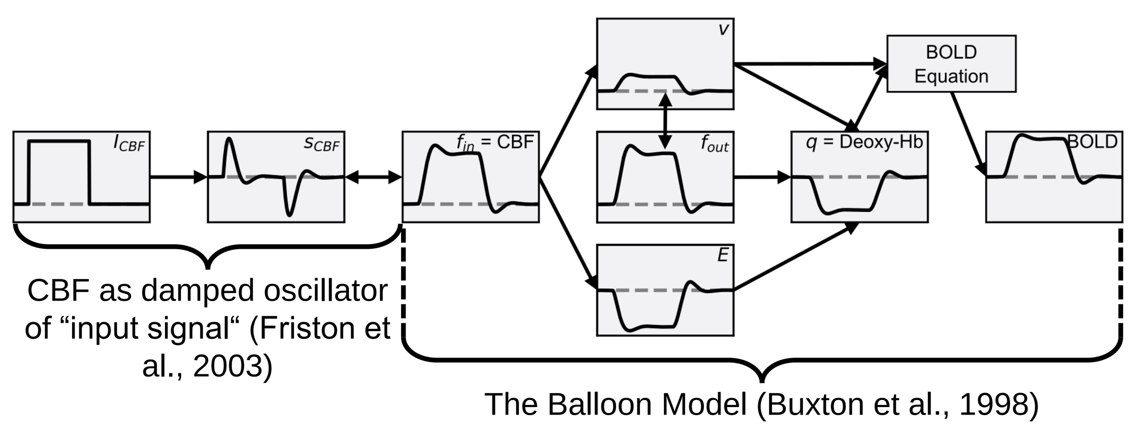



**Simulated BOLD Signals**: Functional magnetic resonance imaging (fMRI) is a widely used method for studying "brain activity". It measures the blood-oxygen-level-dependent (BOLD) signal, which reflects changes in blood flow and oxygenation associated with neural activity. Simulated BOLD signals are essential for comparing model predictions with experimental fMRI data. Furthermore, detailed models simulating BOLD signals can be used to infer underlying neural mechanisms of the fMRI data.

**The Need for Flexible Tools**: Neurovascular coupling, which links neural activity to changes in cerebral blood flow (CBF) and metabolic rate of oxygen (CMRO2), is an active area of research. Recent studies suggest that CBF and CMRO2 may be driven separately by distinct neural processes, which existing simulation tools do not account for. ANNarchy's BOLD monitor provides the flexibility to define custom "BOLD models", allowing the exploration of different hypotheses about neurovascular coupling mechanisms.

**Simulation of Detailed Neural Dynamics:** ANNarchy is designed to simulate neural network models that range from mesoscopic to microscopic levels. These models represent individual neurons and can capture detailed neural processes, including ionic membrane currents and the dynamics of specific classes of real neurons. These detailed models consider more neural mechanisms to which the BOLD signal can be related than the macroscopic models which have been primarily used in imaging analyses.

## BOLD Models - The Balloon Model

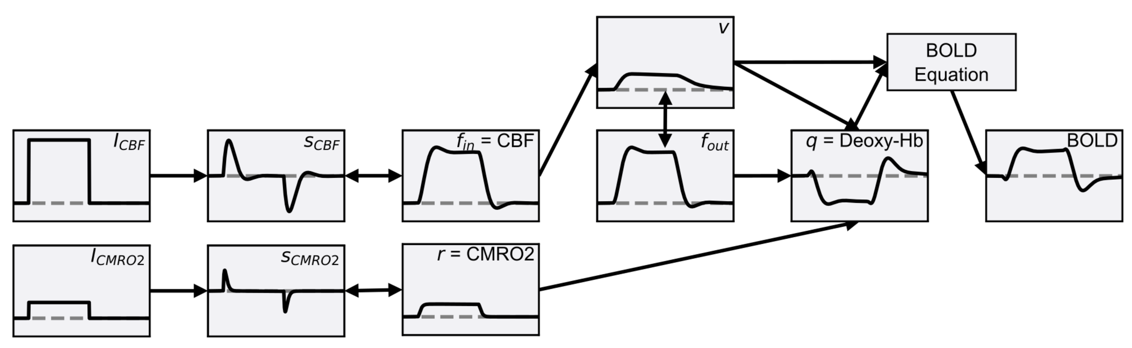



A BOLD model, such as the Balloon model, is a mathematical framework that describes changes in the BOLD signal in a region of interest in response to an "input signal" (i.e. experimental paradigm or network variables like neuronal activity). The Balloon model characterizes changes in the BOLD signal as a function of normalized cerebral blood flow (CBF), normalized deoxyhemoglobin content (q), and the normalized venous volume fraction (v), with the venous volume fraction behaving like a balloon that expands with increased inflow and recovers slowly after.

Equation-based Implementation in ANNarchy:

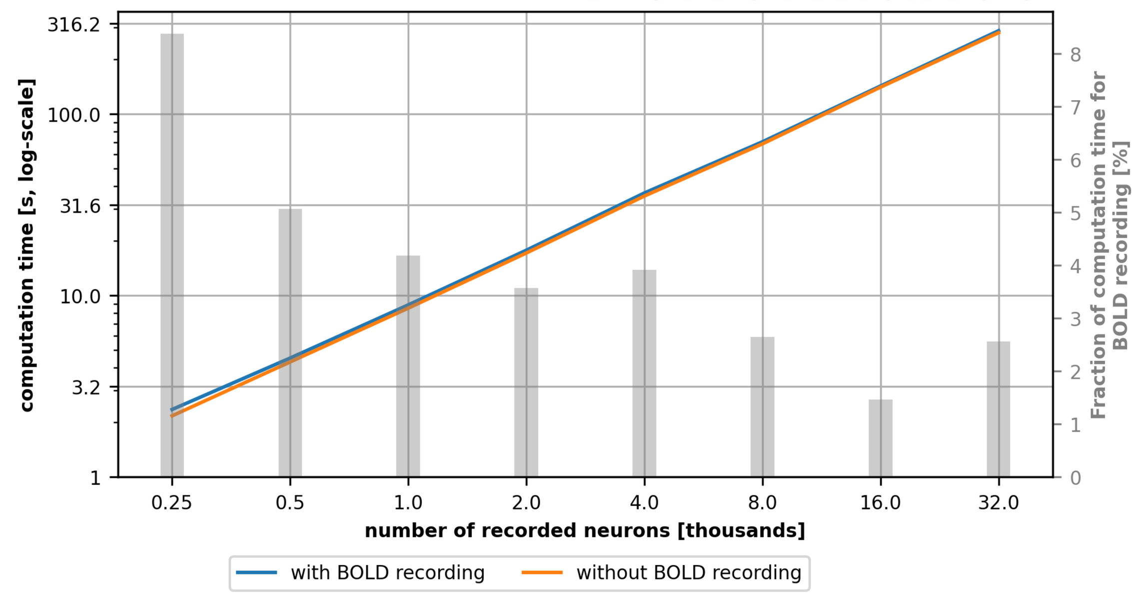
```
balloon_RN = BoldModel(
    parameters = """,
        kappa     = 1/1.54
        ...
    """,
    equations = """
        I_CBF          = sum(I_CBF)                                          : init=0
        ds/dt          = (phi * I_CBF - kappa * s - gamma * (f_in - 1))/second   : init=0
        df_in/dt       = s / second                                          : init=1, min=0.01

        E              = 1 - (1 - E_0)**(1 / f_in)                           : init=0.3424
        dq/dt          = (f_in * E / E_0 - (q / v) * f_out)/(tau*second)     : init=1, min=0.01
        dv/dt          = (f_in - f_out)/(tau*second)                         : init=1, min=0.01
        f_out          = v**(1 / alpha)                                      : init=1, min=0.01

        k_1            = 4.3 * v_0 * E_0 * TE
        k_2            = epsilon * r_0 * E_0 * TE
        k_3            = 1.0 - epsilon
        BOLD           = V_0 * (k_1 * (1 - q) + k_2 * (1 - (q / v)) + k_3 * (1 - v))  : init=0
    """,
    inputs = "I_CBF",
    output = "BOLD",
)
```

ANNarchy allows to implement custom BOLD models.




Based on the "damped oscillator input" idea of Friston et al. (2003) and the separation of CBF and CMRO2 in the Balloon Model according to Buxton et al. (2004), we implemented a 2-input Balloon Model.

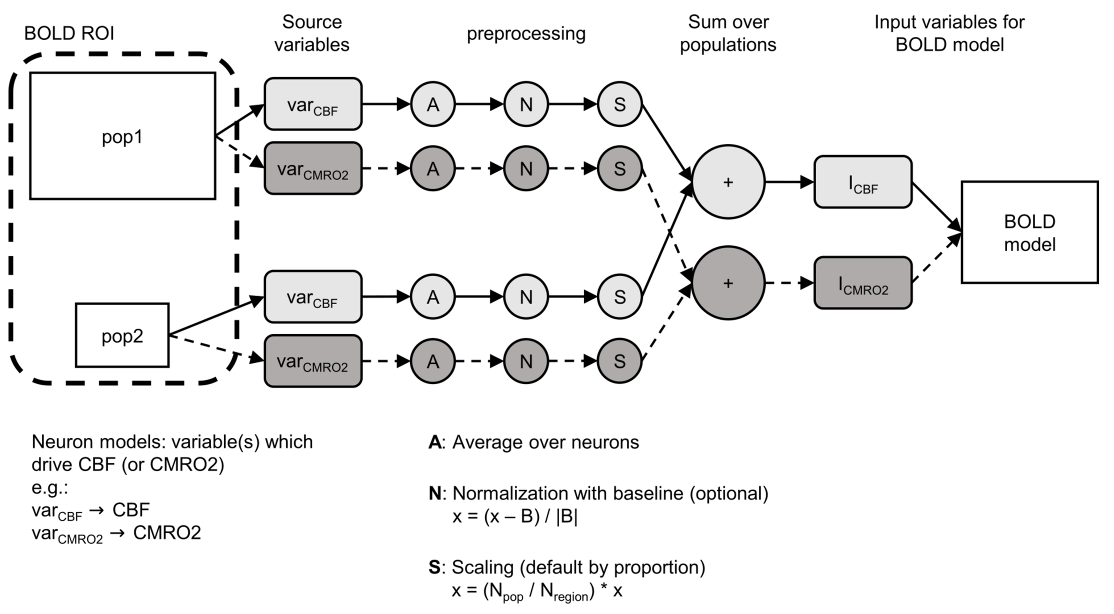
## Performance



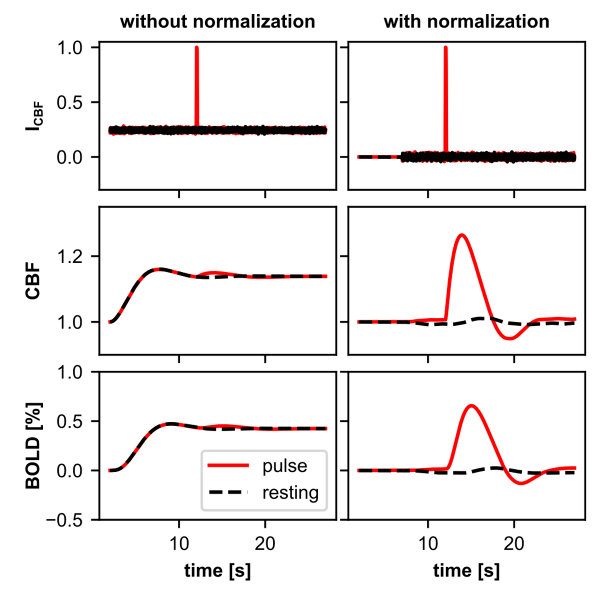

Computation time depending on BOLD computation and the number of recorded neurons. The gray bars indicate the percentage of the computational overhead.

ANNarchy's BOLD Monitor enables on-line BOLD computation, providing access to calculated variables throughout the simulation, reducing memory usage compared to storing the neuron variables and off-line computation. While on-line computation increases computation time, this overhead remains small and even decreases for larger models with more calculations.

## The BOLD Monitor




The connection from the neuronal model to the BOLD model is critical. ANNarchy's BOLD Monitor facilitates the use of neuron model variables as BOLD model inputs. Preprocessing steps simplify ROI definition and signal aggregation into a single BOLD model input.

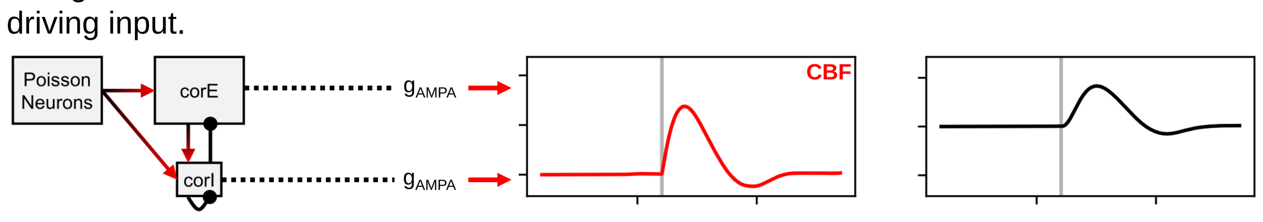



The effect of the baseline normalization. The Balloon model necessitates a signal depicting a departure from a baseline state (=0). Thus, in most cases the normalization is essential when working with the Balloon Model.

## Flexibly Adjust BOLD Computing

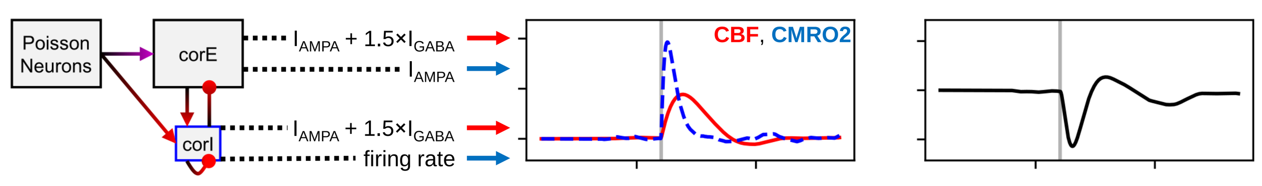
Combining custom BOLD models and the use of neuron model variables as BOLD model inputs results in a highly flexible tool. Here we show two different implementation examples and the effect on the resulting BOLD signal.

Using the "default" i.e. common Balloon model with the AMPA-conductance as CBF-driving input.




```
# f_in = CBF
BoldMonitor(
    populations=[corE, corI],
    normalize_input=baseline_duration,
    mapping={"I_CBF": "g_ampa"},
    bold_model=balloon_RN,
    recorded_variables=["f_in"],
)
```

Using the 2-input Balloon model with AMPA- and GABA-currents as CBF-driving input and distinct CMRO2-driving inputs for excitatory neurons and inhibitory interneurons.




```
# f_in = CBF, r = CMRO2
BoldMonitor(
    populations=[corE, corI],
    normalize_input=baseline_duration,
    mapping={
        "I_CBF": "var_BF",
        "I_CMRO2": "var_O2",
    },
    bold_model=balloon_two_inputs,
    recorded_variables=["f_in", "r"],
)
```

## Conclusions

ANNarchy's BOLD monitor simplifies the integration of common BOLD models (Stephan et al., 2007) through a user-friendly interface. It offers the flexibility of scaling by population sizes and baseline values, facilitating the connection between regions of interest of neural networks and BOLD models. By incorporating BOLD monitoring into ANNarchy, it now enables more detailed model-based inference (i.e. spiking dynamics). Furthermore, for researchers interested in exploring the relationship between neural mechanisms and the BOLD signal, ANNarchy provides a powerful tool that allows for investigations at a scale unmatched by any other neural simulator. We have designed a custom 2-input Balloon Model within ANNarchy and encourage researchers to implement their custom BOLD models and neurovascular coupling mechanisms through the user-friendly equation-based interface.

## References

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