

An Agent-Based Modeling Approach for the Exploration of Topologies of Biological Neural Networks

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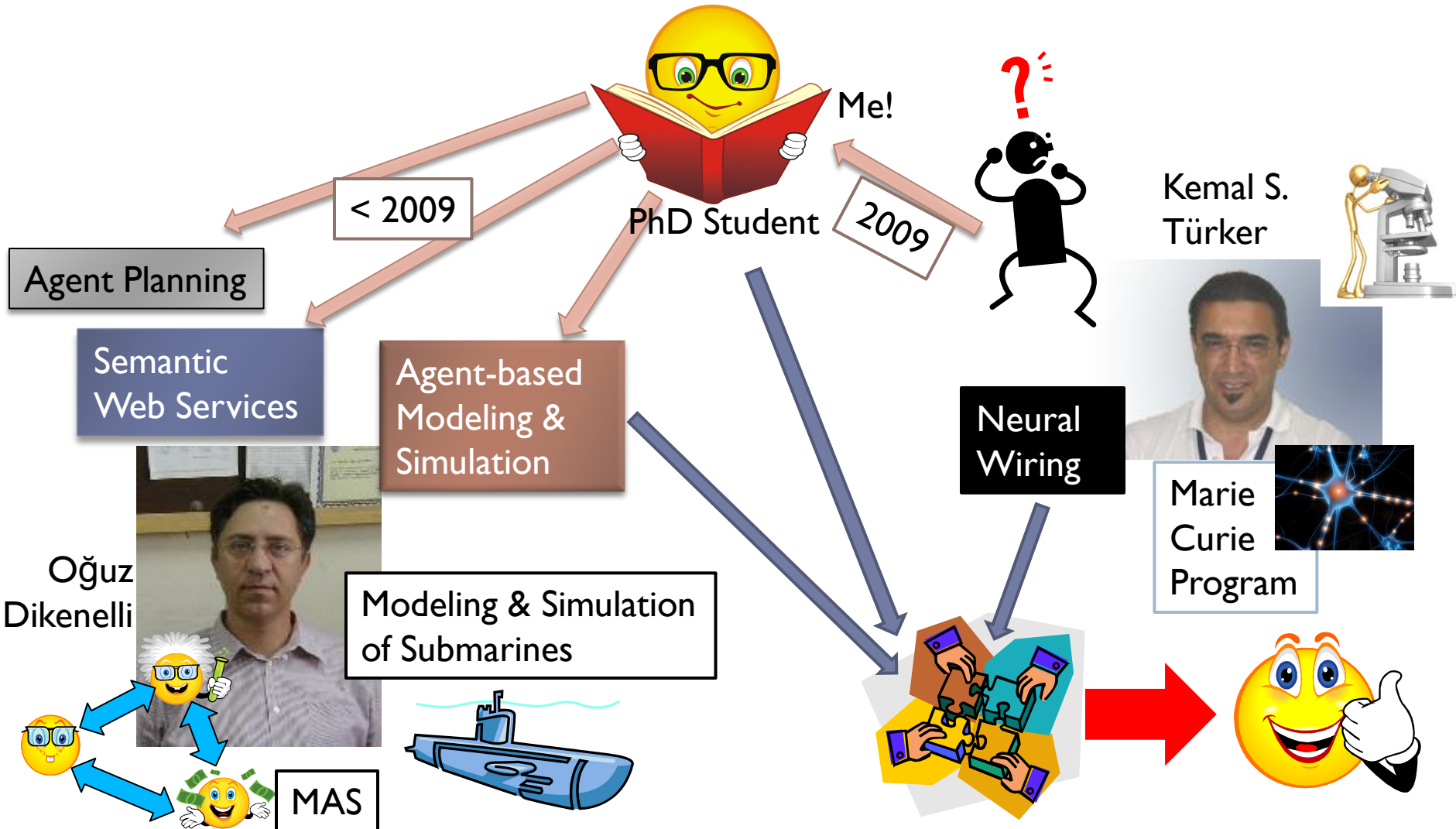
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Su di me!



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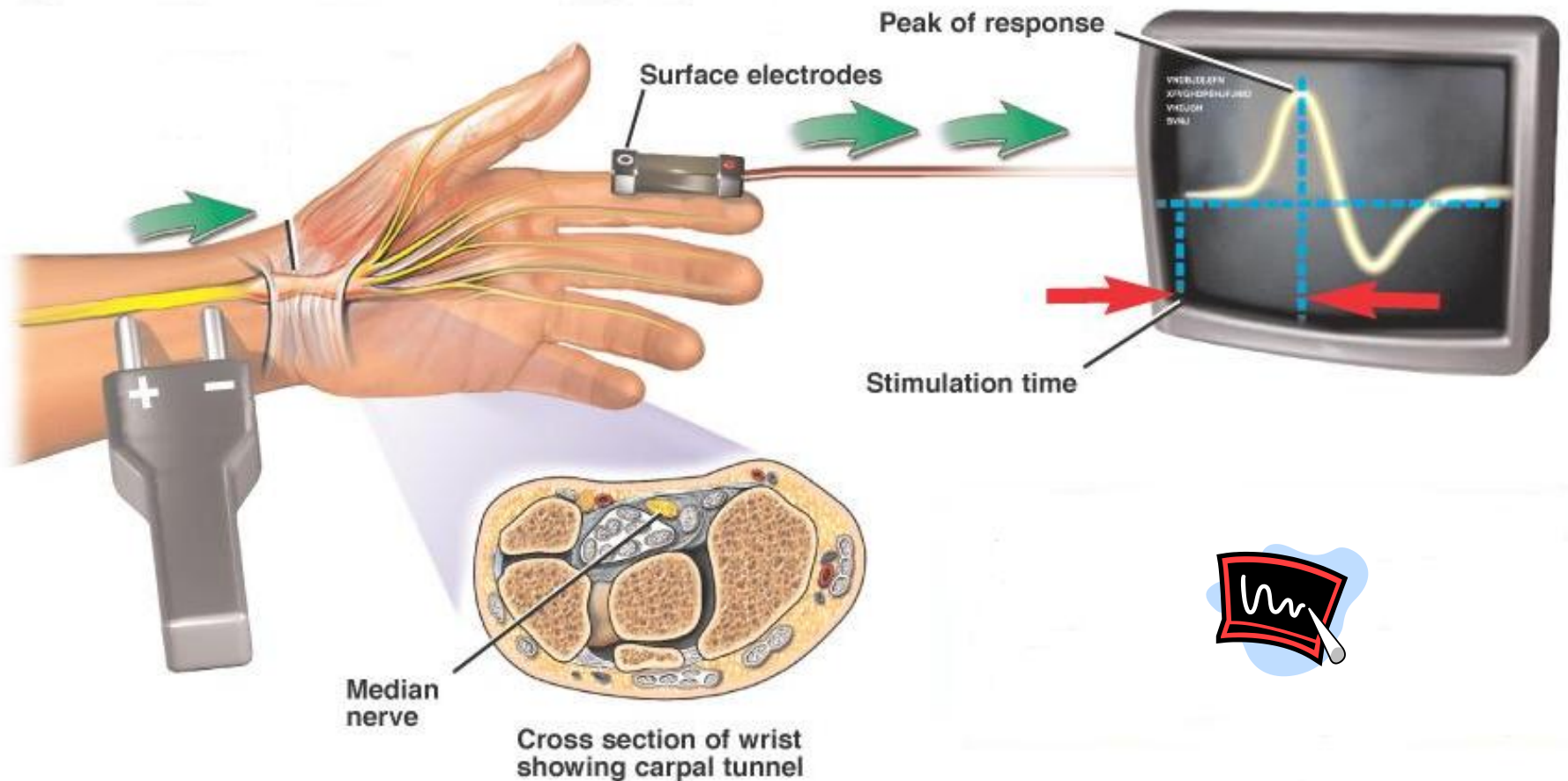
Road Map

- ▶ Introduction
 - ▶ “The Problem”, aims & requirements
- ▶ Related Studies
 - ▶ Toolkits & theoretical studies
- ▶ Our Orientation
 - ▶ What we propose

Introduction

- ▶ The **understanding** of the brain depends on knowledge of its wiring[1].
- ▶ The wiring of the human brain
 - ▶ Direct recording from individual neurons is **impossible**
 - ▶ wiring diagram ~ **black box**
 - ▶ Thus, **indirect** methods!
 - ▶ a particular group of nerve fibres is **stimulated**
 - ▶ the **responses** of neurons that are **affected by** the stimulus are recorded (via electromyogram – EMG)

Indirect Methods (EMG)

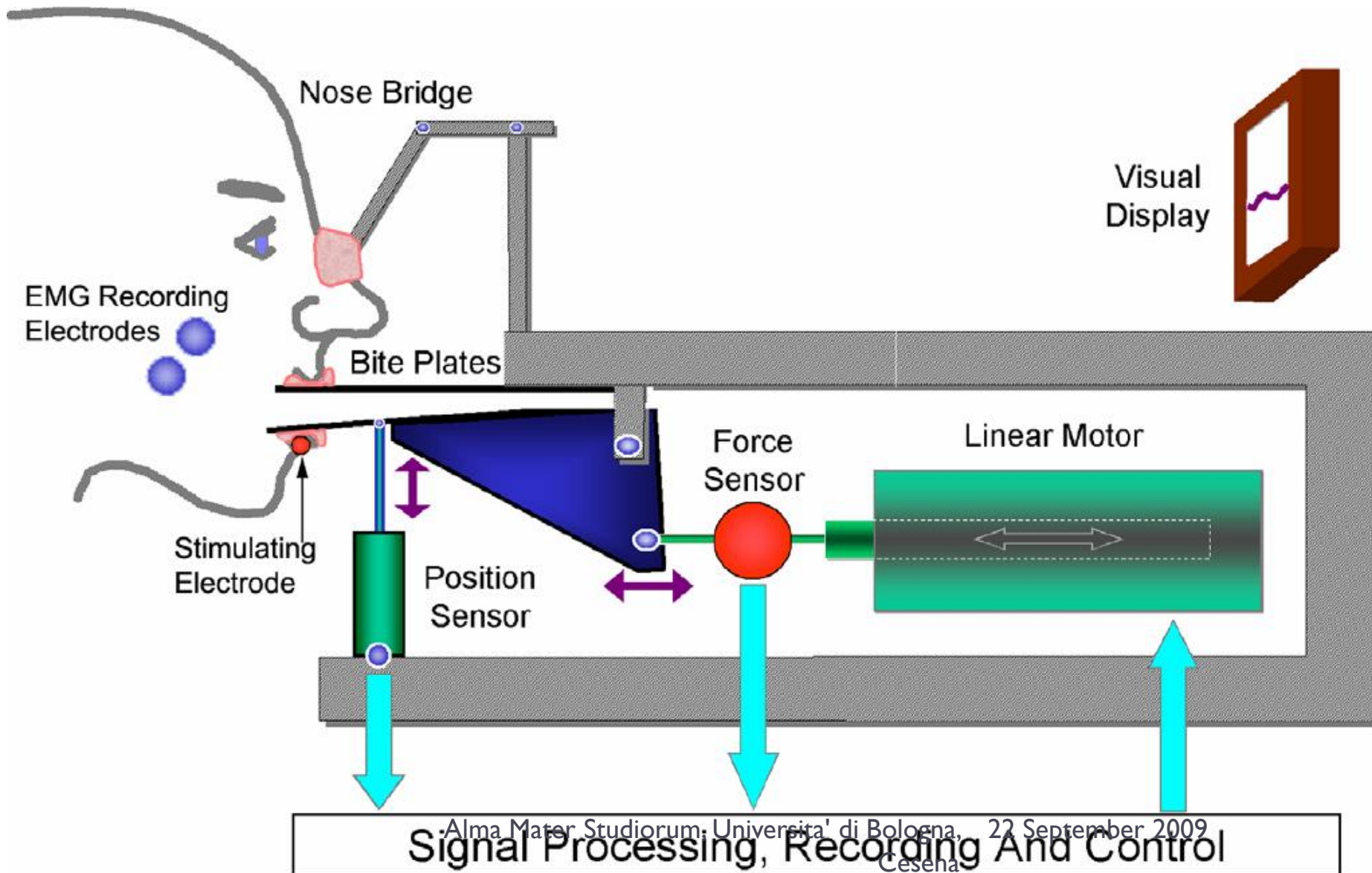


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Problem

- It is **difficult** if not impossible to predict pathways in the CNS **without** direct measurements.
- Indirect measurements (reflex work) contain **significant errors**. (probability based)
- **Error free** indirect estimation of wiring in the human brain has just been tested and now used in Ege University labs. (frequency based)
- Several new studies are now **in progress** that establishes **re-wiring** of the human CNS.
- As **correct pathways** are established, we wish to **combine** the findings into a simulator so that it grows along with the reflex research findings.

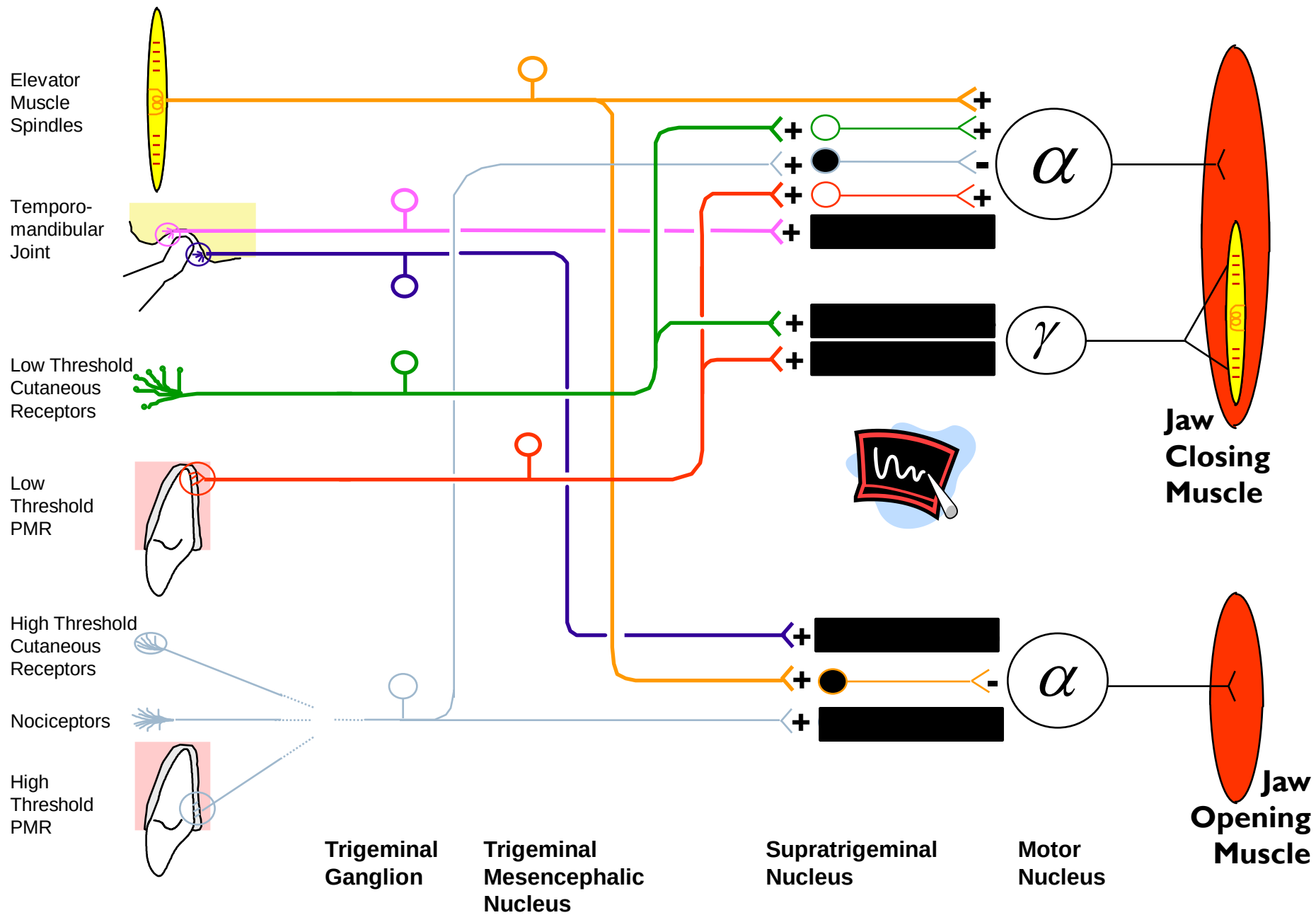
Jaw Reflex Experiments[12]



Jaw Reflex Experiments (cont.)



*Subject bites into his/her impression and **masticates** while upper teeth are tapped with a probe **each time** the jaw passes through as set 'mid-gape' point.*



What we want to do is...

- ▶ To **investigate** functional (not structural) **topologies** of biological neural networks.
- ▶ Develop a tool for **computational experimentation**.

More specifically we want to be able to...

- ▶ **Summate information** available from different resources for different pathways.
- ▶ **Pinpoint gaps** in the system as the final working of the system is known.
- ▶ **Understand** how the central nervous system works.
- ▶ **Bring out** testable **hypotheses** for the unknown sections of the system.

Research Goals

▶ Computer Science

- ▶ Developing a tool using **novel techniques** to **explore the topology** of biological neural networks.

▶ Neuroscience

- ▶ Developing a Biological Neural Network **tool** that allows (computational) **neuroscientists** to explore topologies.
- ▶ **Combining** currently available bits of data into a **manageable** format so that the working of the **entire** nervous system can be **tested**.

▶ Both

- ▶ Demonstrating the **power** of tool through a series of case studies.

Requirements

- ▶ The **model** of a biological neural network should include:
 - ▶ Spiking (**Integrate & Fire**) neuron model
 - ▶ **Reflexes** and their modulations
 - ▶ **Arbitrary** network topologies
 - ▶ **Learning** rules
 - ▶ Hebbian learning, Reinforcement learning or,
 - ▶ More **detailed biological** learning rules
 - Heterosynaptic LTD, Synaptic rescaling
 - ▶ Ability to **adapt** rapid changes in the **neuroscience** research



Related Studies

Artificial Neural Network Toolkits

- ▶ Stuttgart Neural Network Simulator
- ▶ The MatLab Neural Network Toolbox
- ▶ JOONE
- ▶ The NEUROObjects Library
- ▶ Artificial Neural Network Development Environment (ANNDE)

Do not allow arbitrary network topologies

Using neural models of decades ago.

Not suitable for
reflex modulation

Biological Neural Network Simulators

- ▶ Focus on **precise** models of the behavior of a **single** neuron (electrical and chemical signalling in neurons)
 - ▶ GENESIS[7]
 - ▶ NEURON[8]
 - ▶ Nest[11]
- ▶ Focus on functional and developmental neural system simulations (cortical maps)
 - ▶ Topografica[9]
 - ▶ Uses NEST [11]

Not suitable for
network formation

Not suitable for
reflex modulation

Do not support
Spiking Neurons.

Not suitable for exploration of topologies on the fly.

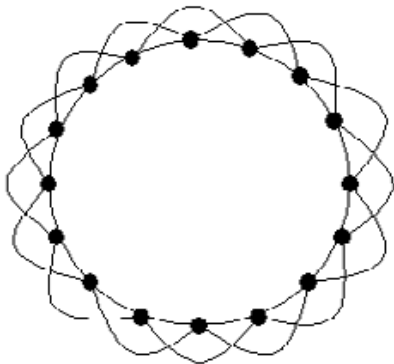
Agent-based Modelling Studies

- ▶ An Agent Based Modeling Approach for the Exploration of Self-Organizing Neural Networks [4]
 - ▶ ABNNSim Toolkit
- ▶ ABNNSim toolkit (**not available!!!**)
 - ▶ Applies agent-based modeling
 - ▶ Simulates biological neural networks
 - ▶ Develops complex network topologies using **pruning**

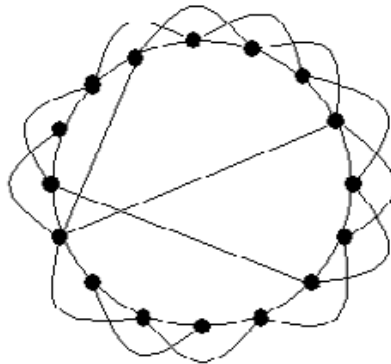


Graph Theoretical Analysis of Structural and Functional Systems [5, 6]

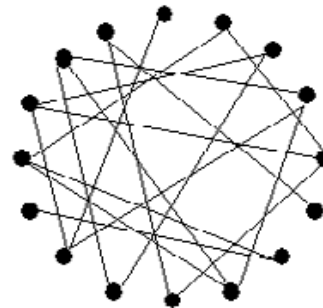
- ▶ Rise of **network science**[3] since mid 1990s.
 - ▶ Driven by the realization that the behaviour of complex systems is **shaped by** interactions **among** their constituent elements.
- ▶ Complex network topologies
 - ▶ ordered, random, scale-free & **small-world**



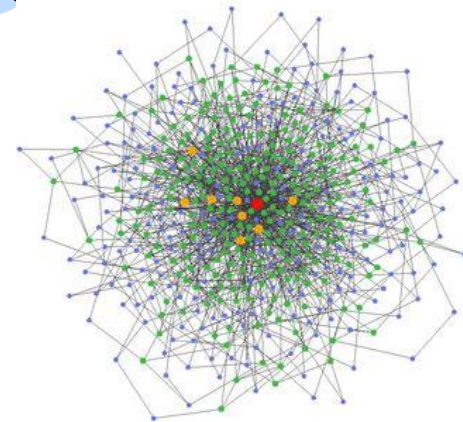
ordered



small-world



random



scale-free

Graph Theoretical Analysis of Structural and Functional Systems [5, 6] (cont.)

- ▶ **Scale-free networks**

- ▶ Internet, Social Networks, Seismological Maps etc.

- ▶ **Small-world networks**

- ▶ Biological neural networks etc.
 - ▶ Recently, **small-world** architectures have been found in several empirical studies of structural and functional brain networks in humans and other animals.
 - ▶ An initially random wiring diagram can evolve **through synaptic plasticity** to a functional state characterized by a small-world topology of the most strong connected nodes and by **self-organized critical dynamics**.

Our Orientation

What We Know

▶ From Neuroscience Studies

- ▶ Behaviors and properties of **individual elements** of CNS
 - ▶ spiking neurons, muscle spindles, muscles etc.
- ▶ ...

▶ From Complex Brain Analysis Studies

- ▶ Topology of biological neural networks => **small-world**
- ▶ random network + **self-organized** dynamics => small-world network

▶ From Computer Science Studies

- ▶ Complex systems can be **understood** by ABMS.
- ▶ Network formation: **pruning & growing approaches**

Our Orientation

Agent-based Modeling and Simulation



Network Science & Graph Theoretical Approaches



Neuroscience Findings

When to use Agent-based Modeling?

- ▶ When the population is **heterogeneous**, when each individual is (potentially) **different**. [2]
- ▶ When the **topology** of interactions is **heterogeneous** and **complex**. [2]
- ▶ When agents exhibit **complex** behaviour, including **learning** and **adaptation**. [2]
- ▶ When there are **decisions** and **behaviours** that can be defined **discretely** (with boundaries). [16]
- ▶ When it is important that agents form **organizations**, and **adaptation** and **learning** are important at the organization level. [16]
- ▶ ...

Also ABMS...

- ▶ Provides more **flexibility**.
- ▶ Allows explicitly representing an **environment**. [17]
- ▶ Allows to model **self-*** (self-organization, etc.)
- ▶ ...

ABMS for Biological Systems

- ▶ For Biological Systems
 - ▶ Agent models has more **biological plausibility!** [13]
- ▶ ABMS is thus **appropriate** as a computer modelling metaphor
 - ▶ for **interdisciplinary collaboration** between modellers and wet lab experimentalists. [13]

ABMS for Biological Systems - Advantages

- ▶ ABMS allows to **predict** behaviour of complex systems.
- ▶ ABMS can be seen as a **substitute** for an experiment **impossible** to make in **reality**. [15]
 - ▶ impossibility can be either **theoretical** or **pragmatical**.
- ▶ Since the theoretical framework is **incomplete** in Biology,
 - ▶ Simulations are used to **test hypotheses** and to **set theoretical** framework. [15]
- ▶ Provides nice **visualizations** which have **meaning to** and **impact on**, biologists. [15]
 - ▶ Which is also useful for **validation**!

ABMS for Biological Systems – Disadvantages

- ▶ **Validation problem [15]**

- ▶ How results of such an (*in virtuo*) experimentation can be **trusted**?
- ▶ We need a **methodology** for validating the results of simulations.
 - ▶ A **tuning** mechanism as described in [14] can be used.



Conclusion

Agent-based Modeling and Simulation

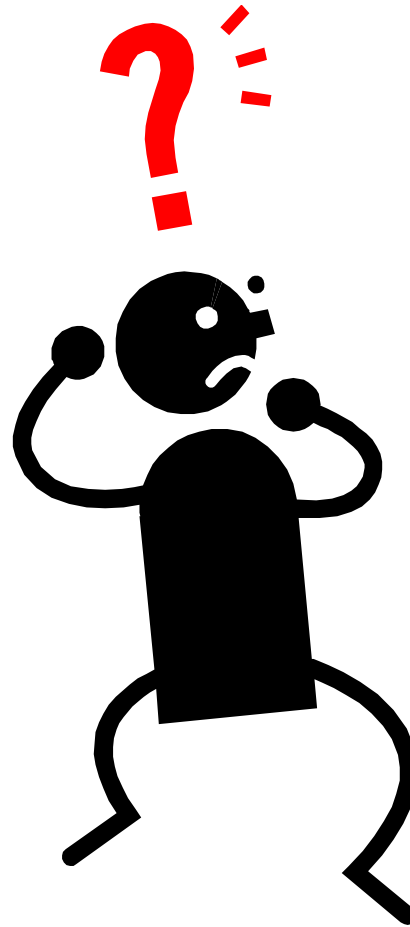


Network Science & Graph Theoretical Approaches



Neuroscience Findings

Thank you all!



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