Cat - Anaesthetised Cat Simulation

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Cat V3.0.0

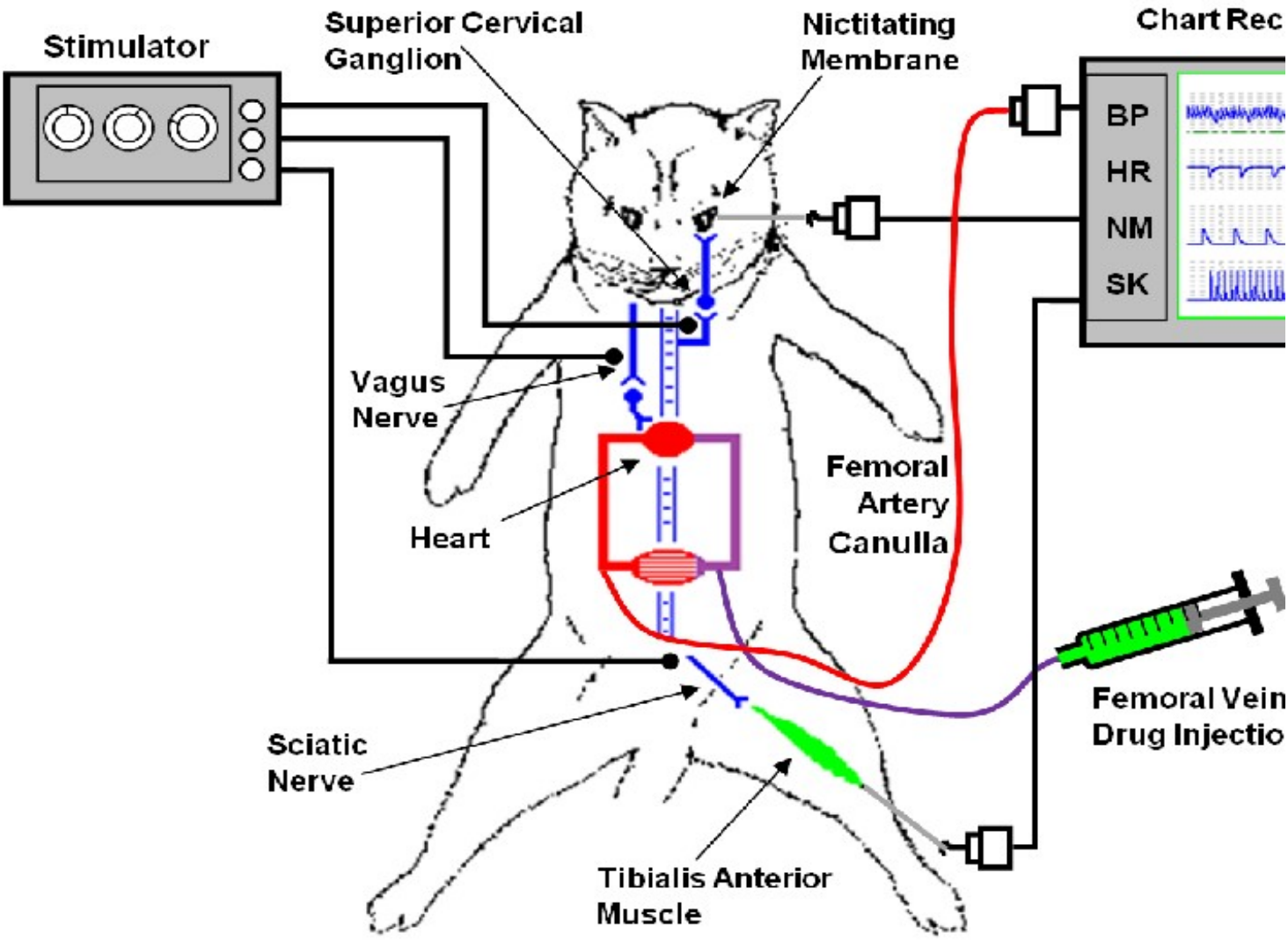
Anaesthetized Cat Simulation

Introduction

The anaesthetised cat is an, *in vivo*, animal preparation which has been widely used as a tool for preclinical studies of the actions of new pharmaceutical compounds on the cardiovascular and skeletal muscle systems, and played an important role in elucidating the mechanisms of action of neuromuscular blocking agents and anti-hypertensive drugs. Compared to studies on isolated cells or tissues, whole animal preparations such as this have the capacity to reveal the multiplicity of effects that a drug can have on different organ systems.

The simulation allows you to observe the cat's **blood pressure** and **heart rate**, **skeletal muscle** and **nictitating membrane** contractions on a simulated chart recorder, and to apply a variety of different drugs and observe their effects.

The preparation



An adult cat is anaesthetised by intraperitoneal injection of a chloralose + pentabarbitone mixture, tracheally intubated, and artificially ventilated. A cannula is inserted into the femoral vein and used to administer drugs. **Arterial blood pressure** is measured via a cannula inserted into the fermoral artery and connected to a pressure transducer.The **heart rate** is derived from this blood pressure signal.

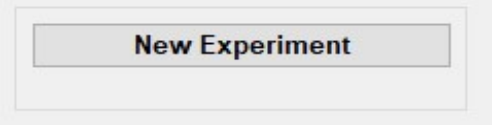
The **vagus nerve** is exposed at the neck (but not cut) and hooked over stimulation electrodes. This nerve innervates the heart, via the ganglion shown. Stimulation causes a reduction in heart rate.

The **cervical sympathetic nerve** is exposed at the neck (ligated preganglionically) and a stimulation electrode attached. This nerve innervates the **nictitating membrane** over the eye of cat, via the **superior cervical ganglion**. The nictitating membrane is attached to a force transducer. Stimulation of the nerve causes a contraction of the membrane.

One end of the **tibialis anterior muscle** (fast type skeletal muscle), in the leg of the cat, is dissected free and attached to a force transducer. The **sciatic nerve** is exposed and attached to stimulation electrodes. Stimulation of the nerve causes contraction of the muscle. The muscle is innervated via nicotinic receptors at the neuromuscular junction.

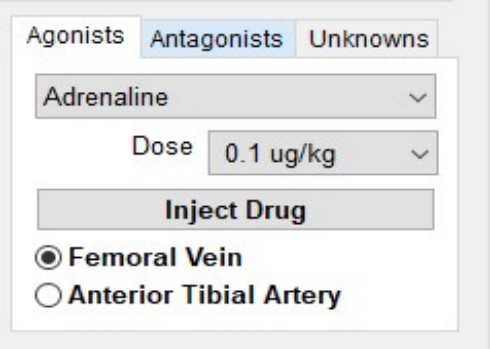
Using the simulation

1) Click **New Experiment** to initiate the experiment. (Note. Clicking New Experiment will clear any existing experimental results from the chart.).



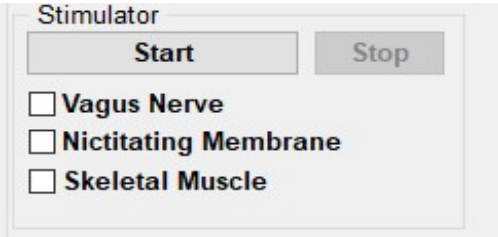
2) Click the **Start** button to start the chart recorder running.

3) To inject a drug into the animal's circulation : select a drug from from either the **Agonist** or **Antagonist** list or an unknown drug from the **Unknowns** list.

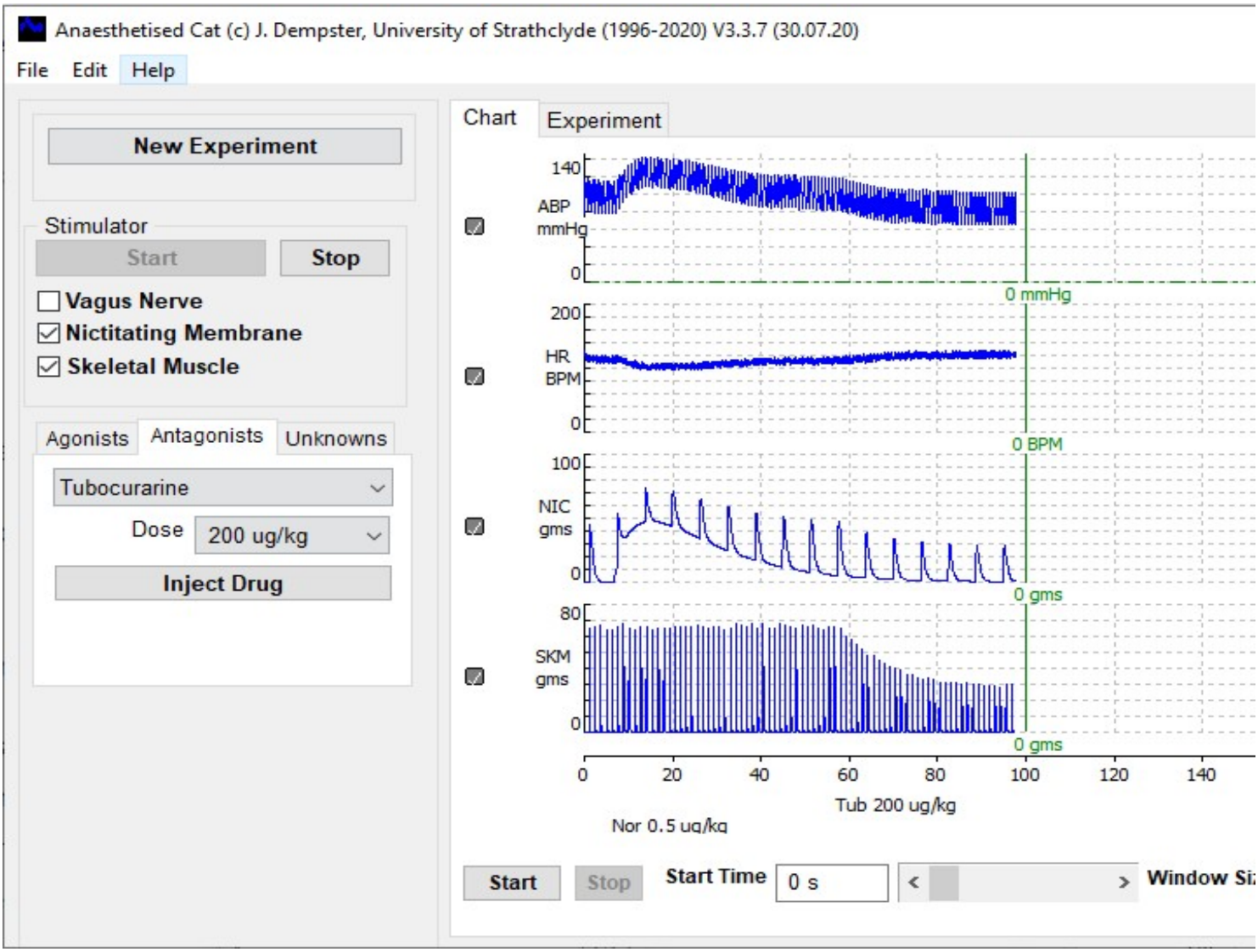


Then select the dose to be injected, the site of injection (**Femoral Vein** or **Anterior Tibial Artery**) and click the **Inject Drug** button. The name and dose of drug injected is indicated on the chart trace.

4) To observe the effect of electrically stimulating various nerve pathways, select the nerve pathway(s) and click the Stimulator **Start** button.



5) You can add as many doses and/or different drugs and/or nerve stimuli as necessary. When you have finished your experiment, click the **Stop** button to stop the chart.



6) You can scroll backwards and forwards through the recording using the slider bar below the chart and/or change the duration of the display window by entering a new value into the **Window Size** box or by clicking the arrow buttons on either side.

7) To make quantitative measurements from the traces, drag the green vertical readout cursor over the trace and note the numerical values of the traces on the display.

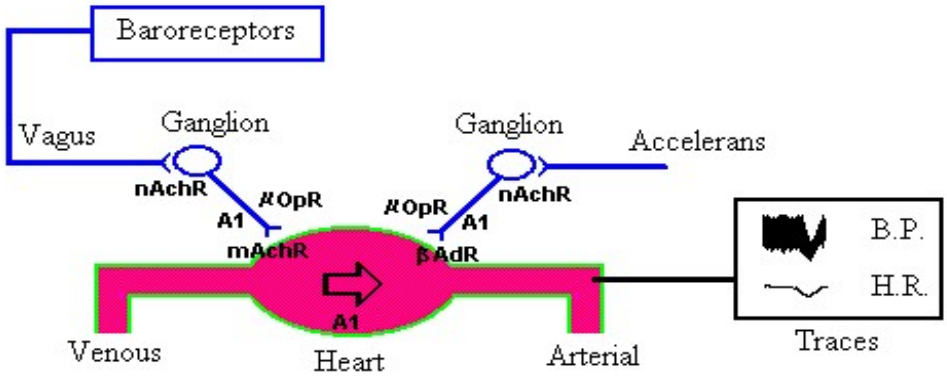
8 To copy a picture of the chart recording to the Windows clipboard for pasting into a report, select **Copy Image** from the **Edit** menu.

9) To print out a hard copy of the chart recording , select **Print** from the **File** menu.

10) When you have completed an experiment you can save it to a storage file by selecting **Save Experiment** ... from the **File** menu. (To re-load an experiment, select **Load Experiment** ...).

11) To exit from the simulation program, select **Exit** from the **File** menu.

The heart and its receptors



The **vagus** nerve releases **acetylcholine** and acts via **muscarinic** cholinoceptors (mAChR) on the heart to **slow** heart rate and **reduce** cardiac force.

The baroreceptor reflex. Baroreceptors within the CNS when stimulated by **high** arterial pressure increase the nerve activity along the vagus **depressing** heart rate and force

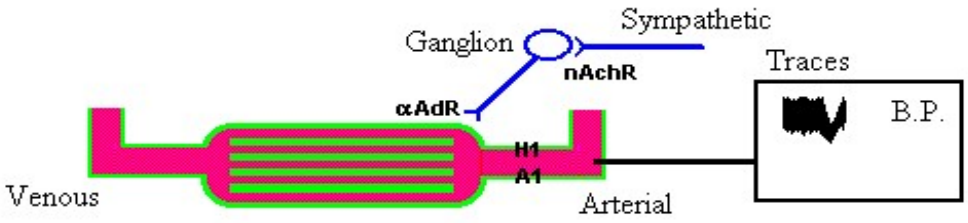
The accelerans nerves releases **noradrenaline** and acts via β**-adrenoceptors** (βAdr) on the heart to **increase** heart rate and contractile force.

Both the vagus and accelerans nerves act indirectly via ganglia. Synaptic transmission. at the ganglia is by **neuronal nicotinic cholinoceptors** (nAChR).

Mu-Opioid and **adenosine** (A1) receptors are present on the presynaptic nerve endings of both the vagus and accelerans nerves and act to **depress** transmitter release.

Heart muscle also has **adenosine** (A1) receptors which cause a **reduction** in heart rate and force in response to circulating adenosine.

The circulation and its receptors



Smooth muscle in the walls of arteries act to **constrict** the vessels. The blood vessels are innervated by **sympathetic** nerves, via **nicotinic ganglia** and are also sensitive to drugs in the circulation.

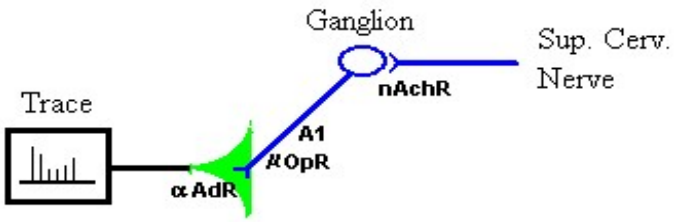
The sympathetic nerves release **noradrenaline** which acts upon α**-adrenoceptors** in the smooth muscle to cause **vasoconstriction** which **increases** blood pressure.

Circulating **acetylcholine** can produce **vasodilatation** by acting upon **muscarinic** receptors on endothelial cells to release vasodilators.

Circulating **adenosine** can produce **vasodilatation** by acting upon adenosine (A1**)** receptors in the smooth muscle.

Circulating **histamine** can produce **vasodilatation** by acting upon histamine (H1) receptors.

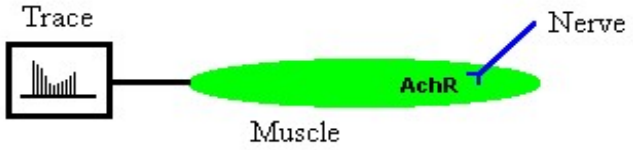
The nictitating membrane and its receptors



The **nictitating membrane** is a protective membrane which can be drawn over the cat's eye. It contains **smooth** muscle and is indirectly innervated by the **superior cervical nerve** via a nicotinic ganglion**.**

The smooth muscle has α**-adrenoceptors** which respond to **noradrenaline** released by the post-ganglionic nerve. Stimulation of the **pre-ganglionic** nerve causes the membrane to contract. The post-ganglionic nerve terminals which release noradrenaline have pre-synaptic **Mu-opioid** (uOpR) and **adenosine** (A1) receptors which act to **depress** transmitter release.

Skeletal muscle and its receptors



The **tibialis anterior** muscle is a fast **skeletal** muscle, innervated by the **sciatic** nerve. Stimulation of the nerve produces a muscle contraction.

The nerve releases **acetylcholine** which acts upon **nicotinic cholinoceptors** (AchR) at the neuromuscular junction to cause contraction.

Note. The muscle does **not** respond to circulating acetylcholine with a contracture since depolarization block occurs (a combination of sodium channel inactivation and receptor desensitization) in response to the slow and prolonged application of acetylcholine. However, rapid injection of Ach into the artery feeding the muscle does cause a contracture.

Drugs

List of drugs available for injection into the cat with the receptors where their primary site of action.

Drug	Receptor
Adrenaline	α+β-adrenoceptor agonist (α=β potency)
Noradrenaline	α+β-adrenoceptor agonist (α>β potency)
Isoprenaline	α+β-adrenoceptor agonist (α<β potency)
Phenylephrine	α-adrenoceptor agonist
Acetylcholine	Cholinoceptor agonist
Suxamethonium	"
Carbachol	"
Histamine	Histamine receptor agonist
Adenosine	Adenosine receptor agonist
Morphine	Opioid receptor agonist
Propanalol	β-adrenoceptor antagonist
Phentolamine	α-adrenoceptor antagonist
Tubocurarine	Nicotinic receptor antagonist
Gallamine	"
Vecuronium	"
Atracurium	"
Hexamethonium	Neuronal nicotinic receptor antagonist
Neostigmine	Cholinesterase inhibitor
Physostigmine	"
Atropine	Muscarinic cholinoceptor antagonist
Mepyramine	Histamine H1 receptor antagonist
Verapamil	Calcium channel blocker.
Naloxone	Opioid receptor antagonist

Acknowledgements

The anaesthetised cat simulation was developed in the 1990s in the Department of Physiology & Pharmacology at the University of Strathclyde to supplement undergraduate experimental pharmacology classes. At the time, an extensive research program using the anaesthetised cat model, lead by Profs. Bill Bowman and Ian G. Marshall, was in progress, assisting the development of new muscle relaxant drugs (Pancuronium, Vecuronium) with the Organon pharmaceutical company. This simulation is based upon the experimental protocols used and the properties of the neuromuscular blocking agents represented derive from these studies. I am grateful to Profs. Bowman and Marshall for their assistance and advice.

References

G. A. SUTHERLAND, I. B. SQUIRE, A. J. GIBB AND I. G.MARSHALL. (1983) NEUROMUSCULAR BLOCKING AND AUTONOMIC EFFECTS OF VECURONIUM AND ATRACURIUM IN THE ANAESTHETIZED CAT. Br. J. Anaesth., 55,1119

G. A. McPherson, E. Malta, C. Raper (1981) Effects of some catecholamines on the cat cardiovascular system: interactions with adrenoceptor antagonists Comparative Study J Cardiovasc. Pharmacol. 3(4):739-52.

W. D. M. PATON AND E. J. ZAIMIS (1951) PARALYSIS OF AUTONOMIC GANGLIA BY METHONIUM SALTS Brit. J. Pharmacol., 6, 155.

W.C. Bowman (1990) Pharmacology of Neuromuscular Function. Butterworth & Co, U.K.

J. W. THOMPSON (1958) STUDIES ON THE RESPONSES OF THE ISOLATED NICTITATING MEMBRANE OF THE CAT J. Physiol. 141, 46-72

Muir AW, Houston J, Marshall RJ, Bowman WC, Marshall IG. (1989) A comparison of the neuromuscular blocking and autonomic effects of two new short-acting muscle relaxants with those of succinylcholine in the anesthetized cat and pig. Anesthesiology. 70(3):533-40.