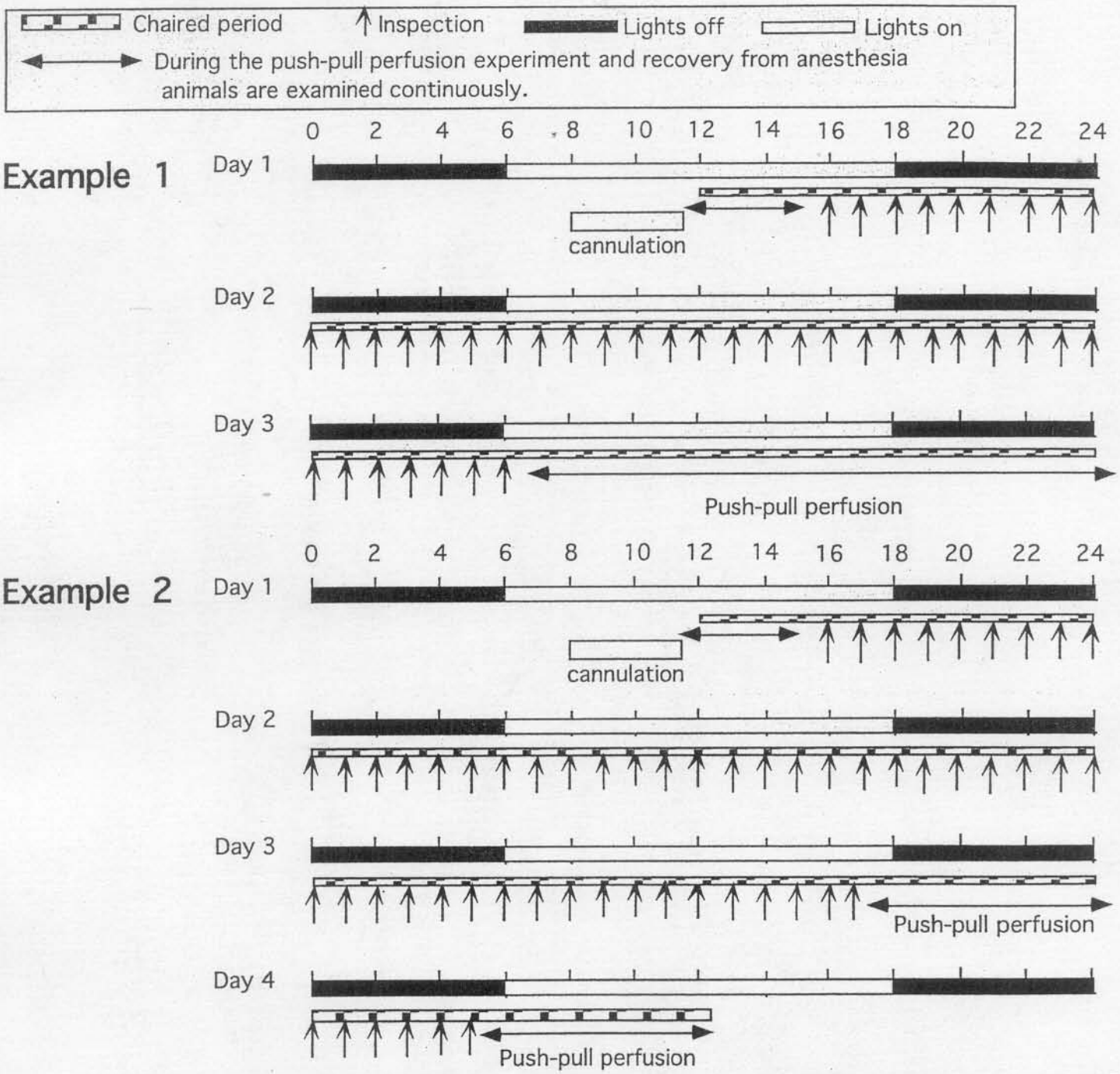
defecation, during the entire experiment will be written on a check sheet on the door and subsequently kept in a file. All procedures are aseptic. Each monkey will have at least a 4-week resting period between push-pull perfusion experiments.

Fig. 1 Schematic illustration of push-pull perfusion experiment.



"Artificial CSF" is a modified Krebs-Ringer phosphate buffer solution composed of 123 mM NaCl, 4.8 mM KCl, 1.22 mM $MgSO_4$, 13.9 mM Na_2HPO_4, 2.45 mM NaH_2PO_4, 1 mM $CaCl_2$, pH=7.4). This formula was established after repeated trials in our laboratory and is not available from commercial sources. We make a 10x concentrated stock solution at monthly intervals. The stock solution is sterilized through a sterile Millipore membrane (0.2μm) and aliquoted into small sterile vials for each use, tightly sealed, and stored in a refrigerator. Prior to infusion, we take a vial, dilute it to the normal (1x) concentration, adjust the pH, and filter again through a sterile Millipore membrane. For all procedures sterile instruments (beakers, pipettes, etc.) are used and water is purchased from UW Pharmacy. This procedure is same as the method for human patients used by Dr. Richard Proctor, Professor of Medical Microbiology and Immunology.

The route and dose of drug administration in the 4 projects are summarized in Table 5. The doses shown are a range of doses that will be tested. It is not possible to include the number of animals per drug and sequence of drugs used for testing in the Table, because: 1) in preliminary experiments we will examine a drug in one or two animals, and if the drug does not cause any effects on LHRH release or GHRH/somatostatin release, we will not examine it further, 2) if preliminary data shows some effects, we will obtain dose response curves, starting at minimum effectiveness in several animals, 3) some drugs cannot be tested at more than one dose in an animal because of receptor desensitization/habituation, whereas some drugs can be tested repeatedly at different doses in an experiment, and 4) some animals will receive more than one drug. Choice of drugs will be made based on the hypothesis to be tested in each project and one animal will receive a maximum of 6 different drugs. Since most of the drugs are very innocuous, and drugs will be infused into the stalk-median eminence directly at doses which are very small, no side effects would occur. In each experiment an average of 3 drugs at different doses will be tested.

Table 5: The route and dose of drug administration:

General category	Drug name	Route	Dose
Catecholamine agonists	methoxamine	Directly to the brain	200-400 μl at 1-100 μM
Catecholamine antagonists	prazosin	Directly to the brain	200-400 μl at 1-100 μM
	Yohimbine	Directly to the brain	200-400 μl at 1-100 μM
GABA agonists	GABA	Directly to the brain	200-400 μl at 10nM-10 μM
	muscimol	Directly to the brain	200-400 μl at 10nM-10 μM
GABA antagonists	bicuculline	Directly to the brain	200-400 μl at 10nM-10 μM
	saclofen	Directly to the brain	200-400 μl at 10nM-10 μM
GABA transporter agonists	GAT-1	Directly to the brain	200-400 μl at 10nM-0.1 mM
GABA transporter antagonist	Gabitril (tiagabine)	Directly to the brain	200-400 μl at 0.1nM-100 μM
	antibody to GAT-1	Directly to the brain	200-400 μl at dilution of 1:100
Glutamate agonists	NMDA	Directly to the brain or i.v.	200-400 μl at 0.1nM-0.01 mM
	Kianate	Directly to the brain	200-400 μl at 0.1nM-0.01 mM
Glutamate antagonists	MK801	Directly to the brain or i.v.	200-400 μl at 0.1nM-0.01 μM
	AP5	Directly to the brain or i.v.	200-400 μl at 0.1nM-0.01 μM
Neuropeptides	LHRH/LHRH agonists	Directly to the brain or i.v.	200-400 μl at 0.1nM-0.1 μM
	LHRH/LHRH antagonists	Directly to the brain or i.v.	200-400 μl at 0.1nM-0.1 μM
	NPY	Directly to the brain	200-400 μl at 1nM-1μM
	Y1 receptor agonists	Directly to the brain	200-400 μl at 1nM-1μM
	Y1 receptor antagonists	Directly to the brain	200-400 μl at 1nM-1μM
	Atrial natriutic peptides	Directly to the brain	200-400 μl at 0.1nM-0.1 μM
	GH releasing peptides	Directly to the brain or i.v.	200-400 μl at 0.1nM-0.1 μM
Oligonucleotides	NPY antisense oligo	Directly to the brain	200-400 μl at 10nM-10μM
	GAD65 antisense oligo	Directly to the brain	200-400 μl at 10nM-10μM
	GAD67 antisense oligo	Directly to the brain	200-400 μl at 10nM-10μM
	GAT-1 antisense oligo	Directly to the brain	200-400 μl at 10nM-10μM
	Somatostatin antisense oligo	Directly to the brain	200-400 μl at 10nM-10μM
Others	ATP/ADP/AMP	Directly to the brain	200-400 μl at 10nM-10μM
	apyrase	Directly to the brain	200-400 μl at 1μM-100μM
	ATP-γ-S	Directly to the brain	200-400 μl at 10nM-10μM
	cyclic AMP	Directly to the brain	200-400 μl at 10nM-10μM
	forskolin	Directly to the brain	200-400 μl at 10nM-10μM
	phorbol ester (PMA)	Directly to the brain	200-400 μl at 10nM-10μM
	prostaglandin E2	Directly to the brain	200-400 μl at 10nM-10μM
	TGFa	Directly to the brain	200-400 μl at 10nM-10μM
	TGFb	Directly to the brain	200-400 μl at 10nM-10μM