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PHYSIOLOGICAL INFLUENCES ON TISSUE ELECTRICAL
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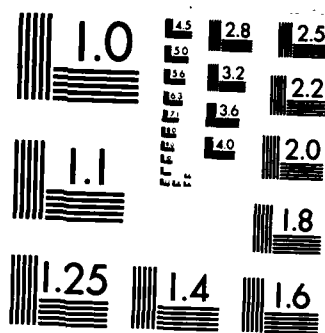
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Annual and Final Report

**PHYSIOLOGICAL INFLUENCES ON TISSUE ELECTRICAL
PROPERTIES IN SITU**

E. C. Burdette
S. R. Crowgey

Contract No. DAMD17-78-C-8044

Supported By
U.S. ARMY MEDICAL RESEARCH AND DEVELOPMENT COMMAND
Fort Detrick, Frederick, Maryland 21701-5012

January 1984

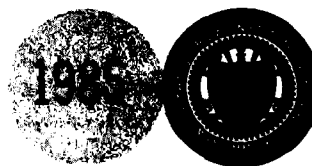
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Measurements of biological tissue dielectric property changes in response to physiological changes may be measured using a small in-situ probe over a wide frequency range. This report describes dielectric property measurements made primarily at 2.45 GHz using a canine brain model and a canine kidney model under varying conditions of perfusion. Experiments during the final year of this program seemed to show some correlation between renal tissue dielectric properties and total renal blood flow under the conditions of pressure-induced blood flow autoregulation, renal nerve stimulation, and pharmacologically-induced		

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Physiological Influences on Tissue Electrical
Properties In Situ



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FOREWORD

This report describes technical efforts undertaken by the staff of the Biomedical Research Division in Georgia Tech's Engineering Experiment Station on Contract No. DAMD17-78-C-8044 with the U.S. Army Medical Research and Development Command. Organizationally, the report first summarizes the major developments during the time period 1 June 1978 to 1 October 1982. This summary is followed by a more detailed description of technical efforts during the period 1 October 1982 through 31 December 1983. Throughout the 4.5-year duration of the contract, research activities were concerned with developing satisfactory techniques for measuring the dielectric property values to determine the nature and extent of changes in physiological functioning.

The research was conducted jointly in the Biomedical Research Division, Electronics and Computer Systems Division, at Georgia Tech and the Physiology Department, School of Medicine, at Emory University. The Principal Investigator was Mr. E. C. Burdette and the Technical Monitor was Dr. Larry Larsen of the Walter Reed Army Institute of Research. Within Georgia Tech, the program was designated Project A-2171. Accomplishments during this program were the result of contributions by many persons. The authors would especially recognize Mr. Fred Cain of the Georgia Tech Research Electronics and Computer Systems Laboratory, Dr. Vojin Popovic of the Emory University Department of Physiology, and both Dr. Larry Larsen and Mr. John Jacobi of the Walter Reed Army Institute of Research, without whom success on this program would not have been possible.

In conducting the research described in this report, the investigator(s) adhered to the "Guide for the Care and Use of Laboratory Animals", prepared by the Committee on Care and Use of Laboratory Animals of the Institute of Laboratory Animal Resources, National Research Council (DHEW Publication No. (NIH) 78-23, Revised 1978).

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SECTION I

INTRODUCTION

Interaction of electromagnetic (EM) fields with a biological system is largely determined by the electrical properties of that system. At radio and microwave frequencies, the dielectric properties are responsible for EM field/tissue interactions. Because of the interaction, accurate in-situ dielectric property information would be of significant benefit in many dosimetric and diagnostic applications. Real-time in-situ measurements in living tissues could be used for the detection of pathophysiological conditions in tissues, for measuring changes in certain normal physiological processes, for differentiating between normal and diseased tissues, for measuring relative blood flow, and for elucidating pharmaco-physiological effects due to drugs. Tissue dielectric properties also play a key role in electromagnetic imaging, whether for dosimetric or diagnostic purposes. Specific differences or dynamic changes in in-situ dielectric properties within a single tissue type or among tissues reflect the ability of EM imaging methods to discern the existence of pathophysiological conditions (in addition to determining dielectric boundary locations) in intact tissues, organs, or organisms. Differences between in-situ living tissue properties and in-vitro properties are of key importance in dosimetry determinations (in both magnitude and distribution) via EM imagery [1-4]. Finally, in dosimetry determinations with respect to potential EM radiation hazards and in treatment planning for cancer patients using hyperthermia induced by electromagnetic fields, an accurate knowledge of the respective in-situ tissue dielectric properties is essential to accurately determining absorbed power [5].

In the past, determination of the dielectric properties of biological tissues has been limited to measurements over restricted frequency ranges on excised tissue samples. These previous results served to validate electrical impedance models of tissue structure, but were not capable of yielding information on the actual living in-situ tissue electrical properties. In addition, the influence of surrounding tissue organization, blood perfusion, and the development of pathological conditions could not be ascertained from these in-vitro measurements.

At high frequencies, it is known that bulk tissue dielectric characteristics largely reflect those of water. However, in measurements

performed in-situ (under the present contract), changes in the dielectric characteristics of brain tissue at microwave frequencies were seen immediately upon termination of the experimental animal [6,7]. These initial changes were followed by a slower, gradual reduction in permittivity and conductivity over a longer period of time (two hours). The initial change was attributed to blood loss, while the slower changes were attributed to a combination of tissue water loss and autolysis. From those in-situ studies of permittivity, there appear to be significant influences on tissue dielectric characteristics, even at microwave frequencies.

Extensive work at Georgia Tech has been devoted to studying and developing a small (2mm diameter) probe that operates over a wide frequency range (1 MHz to 10,000 MHz) [6-9]. The development of this measurement probe provides the opportunity for obtaining in-situ dielectric data over a range of physiological conditions and offers the potential of using dielectric measurements for the detection of local tissue pathology. With this probe technique, it was also possible to determine that the time rate of change of the in-vivo tissue dielectric properties correlated well with changes in tissue blood flow.

During the present program, under the U.S. Army Medical Research and Development Command support, the measurement capabilities of the in-situ dielectric probe have been significantly improved [6,10,11]. The versatility of the probe was increased through the use of a high-quality flexible probe cable, and systemic and cable/connector measurement errors were accounted for through the development and application of a data correction and processing program which corrects the impedance data measured by the probe for those errors. Methods were developed to eliminate fluid accumulation at the tip of the measurement probe, thereby improving measurement accuracy and repeatability. An investigation to determine the minimum sample volume necessary for accurate dielectric measurement results was conducted for probes having diameters over the 1.1 mm to 6.0 mm range. Techniques for rapid data acquisition and processing were studied and developed, and two types of probe holders (for single probes and multiple probes) which maintain the probe contact pressure on the tissue being measured at a nearly constant value were developed and tested. In-situ measurements of different locations within dog brain were performed which yielded information about the existence of significantly different dielectric properties for the various types of brain matter, which in turn impacts EM-hazards dosimetry determination.

Several investigations of physiological significance were performed during this research program. One major study conducted involved the effect of physiological changes at death on in-situ dielectric properties. The results of antemortem/postmortem experiments using two methods of sacrifice (KCl and CaCl_2) were reported in Annual Report dated September 1980 [10]. Significant dielectric changes occurred postmortem for both KCl and CaCl_2 sacrifice, with differences between the two sacrificial methods being observed. Measurement of in-situ dielectric changes during death were also performed in canine gray and white matter. Changes in in-situ dielectric impedance due to the presence of vasculature at the probe measurement site were examined during in-situ measurements on the pia mater of canine brains. Other investigations included experiments involving measurement of in-situ dielectric properties of the auditory cortex during acoustical stimulation 6,10 .

Results of dielectric measurements of renal tissue under controlled perfusion conditions in-vitro consistently showed a proportional relationship between renal flow and relative permittivity and conductivity [12]. For both cortical and medullary tissues, autoregulation of renal flow was observed and dielectric property changes followed the autoregulatory curve. Cortex and medulla tissues exhibited dielectric changes in the same direction; although cortical changes were generally greater. Radioactive tracer studies, performed using an Anger camera to image injected boluses of free Technetium, were used to confirm that dielectric changes closely followed regional renal flow rate changes, with little or no dielectric change being observed at perfusion pressures where flow autoregulation occurred. Regional dielectric and flow changes in cortex and medulla were similar in nature, but autoregulation was observed at different flow rates in the two regions.

During the present year, emphasis has been placed on the further examination of the physiological relevance of dielectric property changes in living tissues. Studies have included the investigation (1) of the influences of renal sympathetic nerve stimulation on renal blood flow and renal dielectric properties, (2) of pharmacological influences on renal flow and dielectric properties, (3) of changes in renal tubular absorption and secretion, and therefore, tubular flow, on medullary dielectric properties, and (4) of brain dielectric properties measured under conditions of changed cerebral blood flow.

These developments, i.e., the improved in-situ probe measurement technique itself and the important new data which reflect the influence of changing physiological conditions on tissue electrical properties, represent significant advances toward an ability to characterize the functional status of living biological systems with respect to medical applications of EM energy and to EM dosimetry.

SECTION II

RESEARCH EFFORTS DURING THE PERIOD 1 JUNE 1978 to 1 OCTOBER 1982

During the period 1 June 1978 to 1 October 1982, under the U.S. Army Medical Research and Development Command support, the measurement capabilities of the in-situ probe dielectric measurement method were significantly improved. The versatility of the probe was increased through the use of a high-quality flexible probe cable, and systemic and cable/connector measurement errors were accounted for through the development and application of a data correction and processing program which corrects the impedance data measured by the probe for those errors. Methods were developed to reduce fluid accumulation at the tip of the measurement probe, and an investigation to determine the minimum sample volume necessary for accurate dielectric measurement results was performed. Techniques for rapid data acquisition and processing were studied and developed, and both single and multiple probe holders which maintain the probe contact force on the tissue being measured at a nearly constant value were developed and tested. In-situ measurements of different locations within dog brain were performed which yielded information about the existence of significantly different dielectric properties for the various types of brain matter, which in turn impacts EM-hazards dosimetry determination. Studies of antemortem/postmortem dielectric characteristics of the pial surface of dog brain, investigation of renal dielectric properties under conditions of altered renal blood flow, and studies of renal flow autoregulation and dielectric properties in kidney cortex and medulla were performed.

The first year of this research program was largely devoted to further development of the in-situ probe dielectric measurement technique. Under previous research efforts [6,9], it was determined that probe positioning was a critical factor in the performance of accurate in-vivo dielectric measurements. Further, it was determined that positioning of the probe needed to be made more compatible with measurements of relatively large animals (i.e., dogs, as opposed to mice or rats). Several alternative methods involving the use of semi-rigid or flexible coaxial cable attached to the in-vivo measurement probe were evaluated. The technical requirements of a suitable cable for use with the probe were the following: a length adequate to

allow the probe to be positioned on a large experimental animal (dog) and still permit convenient location of the network analyzer, adequate cable flexibility for ease in repositioning, introduction of minimal phase variations due to cable movement, low attenuation and VSWR, and the ability to withstand sterilization. Following an examination of cables from nearly a dozen manufacturers, it was determined that the best-suited cable was the Gore-Tex flexible cable. A three-foot length cable, including connectors, was tested and found to perform satisfactorily over the frequency range examined (2-4 GHz).

An investigation of the accuracy of the results obtained from measurements of standard dielectric materials indicated a need to evaluate the residual systemic errors associated with the network analyzer measurement system [8]. An existing model [6,9] for reduction of microwave measurement errors (directivity, source match, frequency tracking) associated with the network analyzer, reflectometer, and interconnecting cables was further developed to include multiple-load data in the determination of the directivity error. Also, the systemic error correction model was incorporated in a microprocessor-based data acquisition/data processing system. The error correction is performed through measurements of terminations (short circuits, open circuit, and a sliding matching load) for which the reflection coefficients are known. From these measurements, the error terms are computed using the error correction model and the measured tissue sample data are corrected to account for the systemic measurement errors. Reflection coefficient data from test samples measured by the probe are automatically collected and processed, and corrected dielectric property information outputted. Measurements may be made either over swept frequency bands between 0.11 GHz and 10 GHz or as a function of time at a single frequency.

Studies of antemortem/postmortem dielectric property changes in dog brain were conducted during the second year, and a limited investigation of vascular effects on measured in-situ tissue impedance was performed [10]. Each of the antemortem/postmortem experiments involved measurement of the in-situ dielectric properties of dog brain with the dura mater and arachnoid removed and the probe placed directly on the pia mater over the ectosylvian gyrus. All dielectric measurements were performed as a function of time at a frequency of 2450 MHz using a 2.1 mm diameter probe.

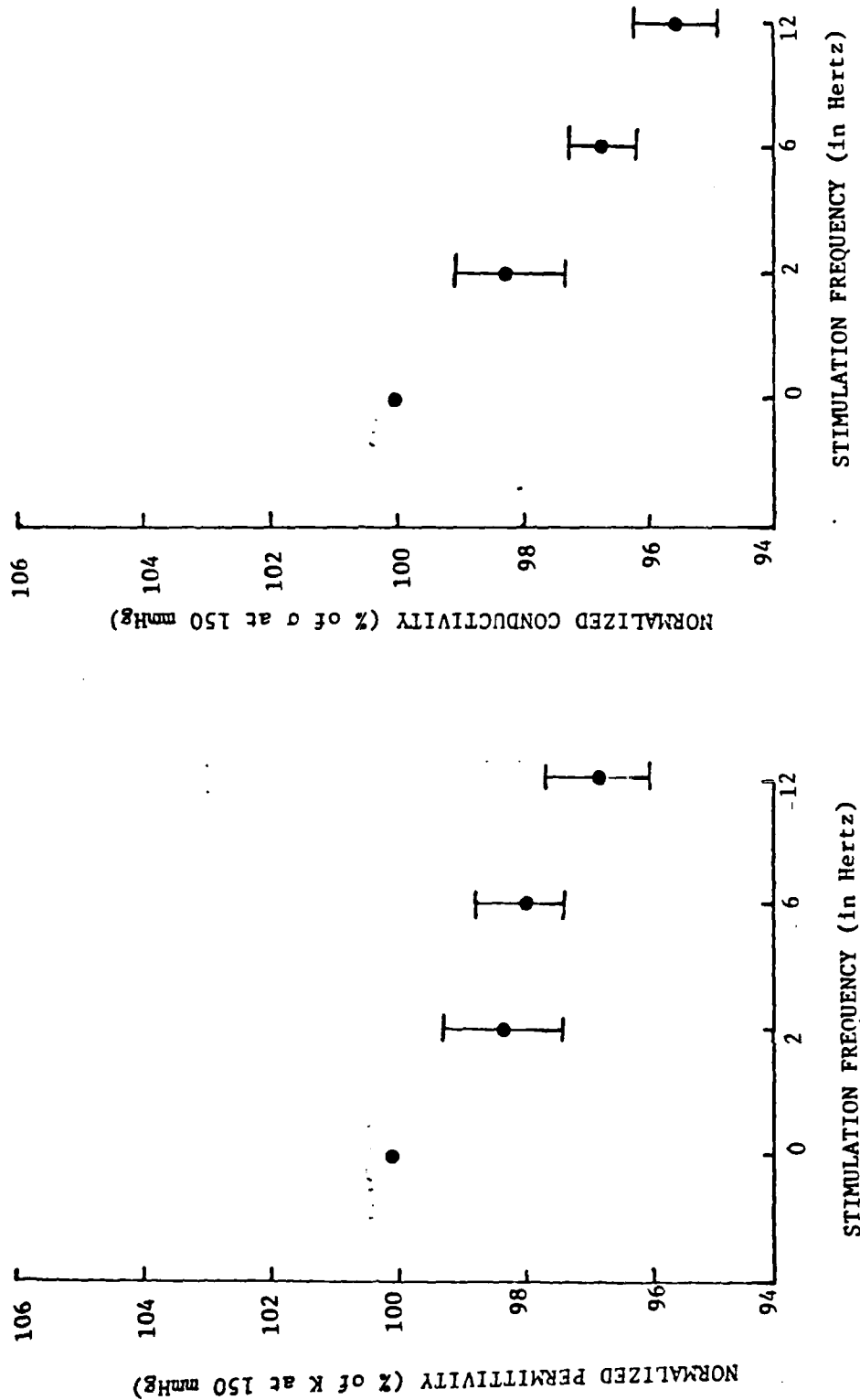


Figure 8. (a) Normalized permittivity, K , and (b) normalized conductivity, σ , as a function of renal nerve stimulation frequency (stimulation intensity, 5V; 5 ms duration).

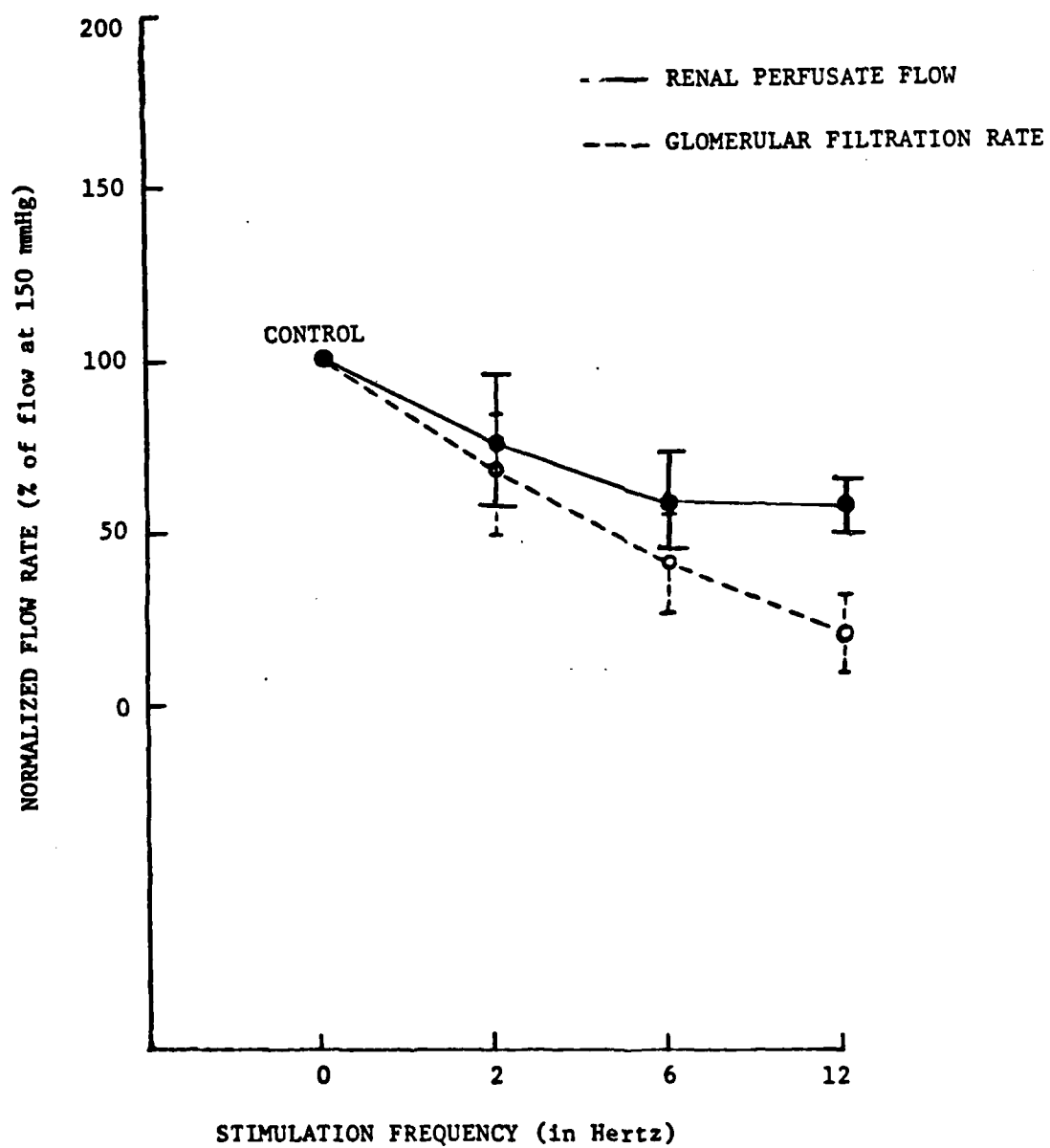


Figure 7. Normalized flow rate as a function of stimulation frequency (stimulation intensity:5V) for three kidneys.

A series of experiments designed to examine sympathetic nerve stimulation effects on renal flow also were conducted. The decentralized renal nerves of dog kidneys were stimulated at frequencies of 2, 6, and 12 Hz while monitoring changes in RPF, GFR, and renal dielectric properties. The responses in four kidneys perfused at a constant renal perfusion pressure (RPP) of 150 ± 9 mm Hg are presented in Figure 7. Control values of all parameters prior to and following stimulation are also indicated. Relatively small changes in renal hemodynamics were observed at the 2 Hz stimulus frequency. Only minor perfusion circuit resistance changes were needed to maintain RPP at or near 150 mm Hg. At stimulus frequencies of 6 and 12 Hz, more significant responses in all parameters measured were observed and maintenance of RPP near control values required that the adjustable in-line circuit resistance be increased (in order to decrease RPP). Using this approach, it was possible to hold the perfusion pressure relatively constant near 150 mm Hg. Increasing the stimulus frequency produced increased renal vasoconstriction with correspondingly larger increases in resistance being required to maintain constant RPP. At a stimulus frequency of 12 Hz, RPF was reduced to 52% of control values and changes in relative dielectric constant and conductivity were 3.7% and 4.1%, respectively. These results are shown in Figure 8. The renal vascular response began within 1-2 seconds after onset of stimulation and was maximum 40-50 seconds after beginning stimulation. Stimulation was usually halted after 90 seconds and RPF returned to control values within 60-90 seconds. GFR decreased with increasing stimulation frequency as did RPF, however, GFR was apparently more sensitive to stimulation at higher frequencies than was RPF. At 12 Hz, GFR was reduced to approximately 18-20% of control values. Measured changes in relative dielectric constant and conductivity closely followed the changes in RPF, returning to initial values shortly after cessation of stimulation. It is readily observed from the results shown in Figures 7 and 8 that the renal vascular response to graded renal sympathetic nerve stimulation and the renal dielectric response correspond closely with each other. Although the dielectric property changes are not as great as the renal vascular changes, they are great enough to be readily measured and to establish significance. An ability to use such information to follow/measure physiological changes is very important in establishing electromagnetic diagnostic methods.

Alpha adrenergic blockade with phentolamine in three kidneys produced renal vasodilation and a sudden decrease in RPP. Perfusion pressure was

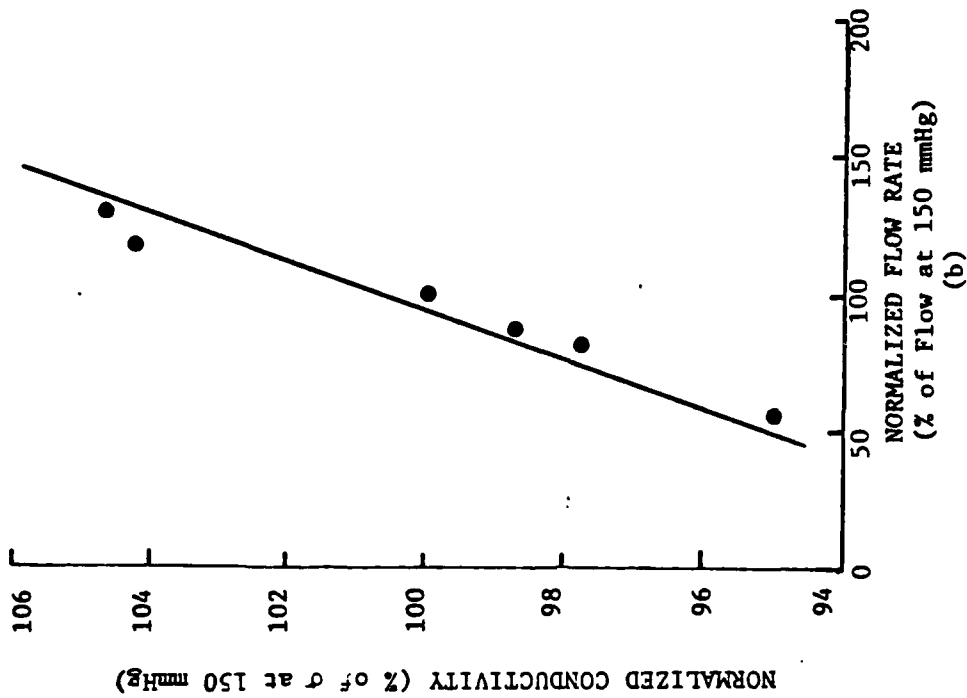
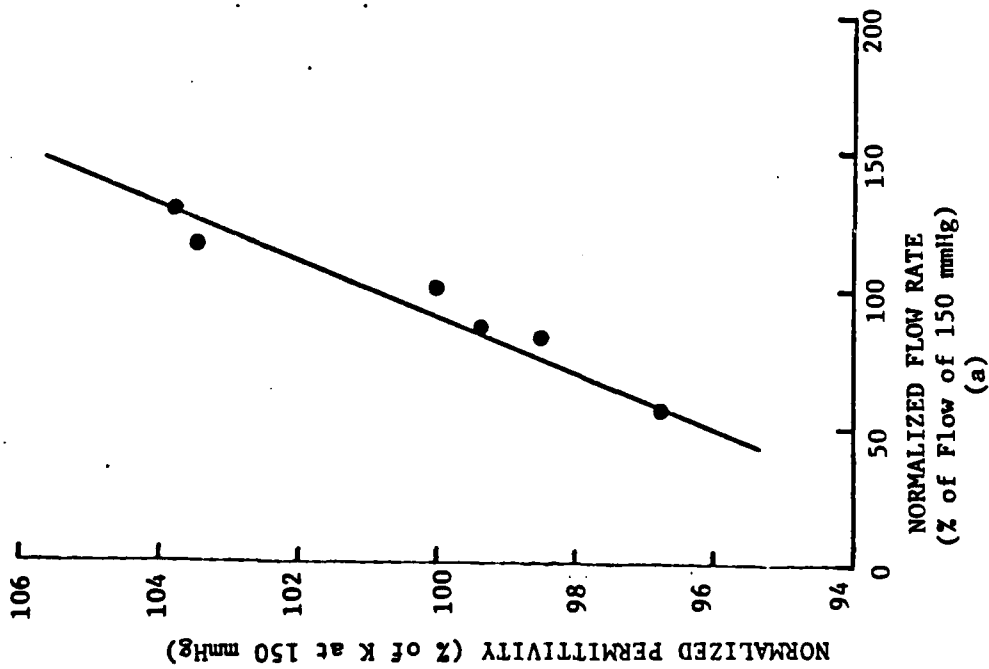
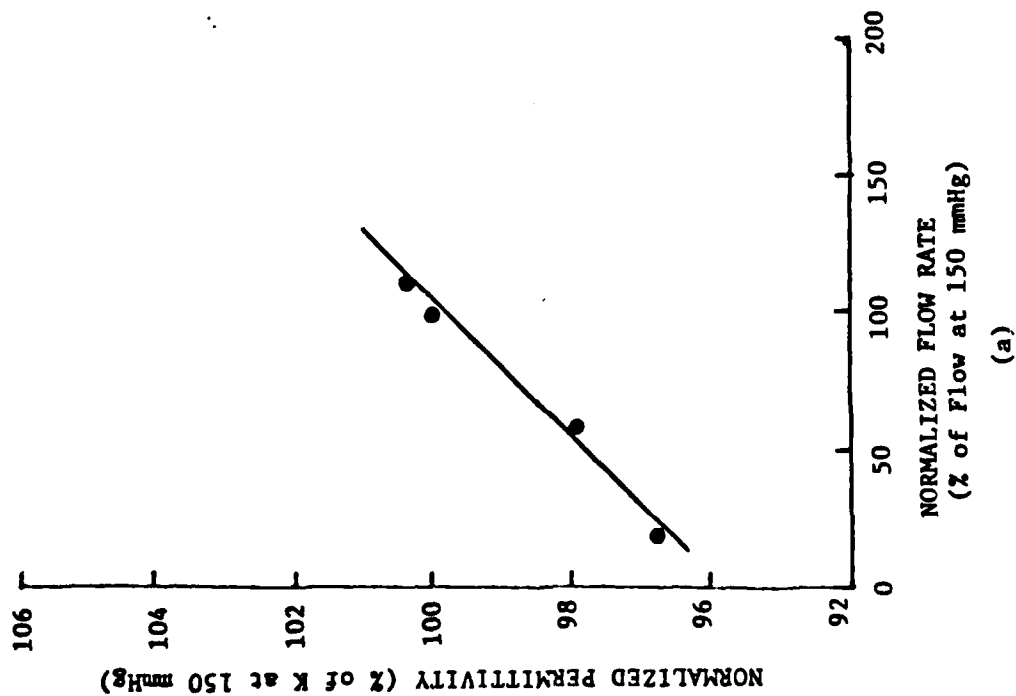
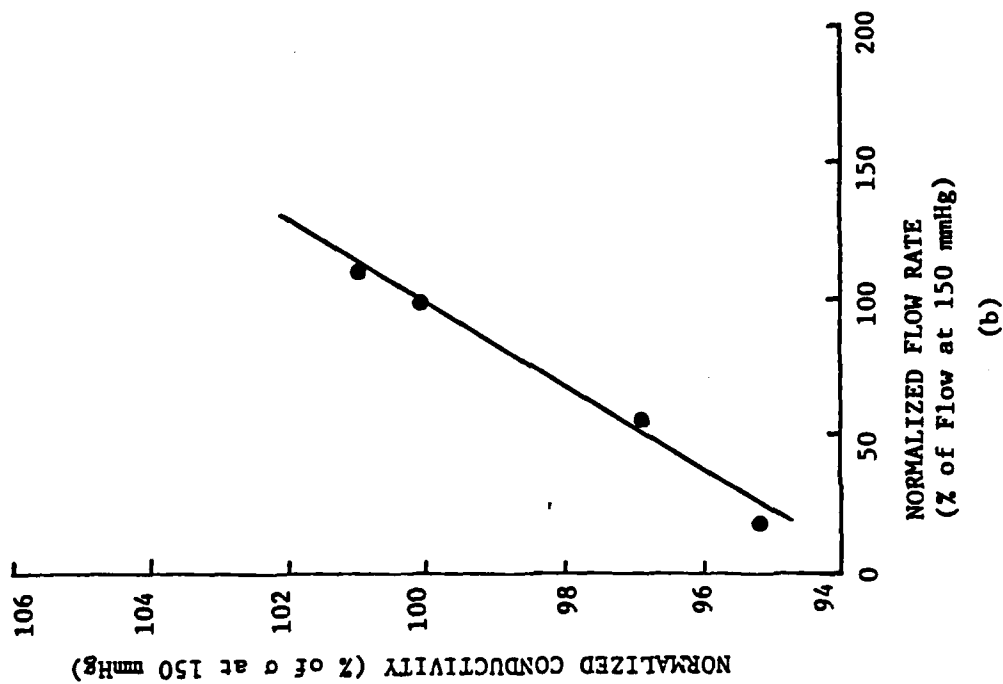


Figure 6. (a) Normalized permittivity, K and (b) normalized conductivity, σ , the normalized flow rate for the case shown in Figure 4.



(a)



(b)

Figure 5. (a) Normalized permittivity, K , and (b) normalized conductivity, σ , as a function of normalized flow rate for the case shown in Figure 3.

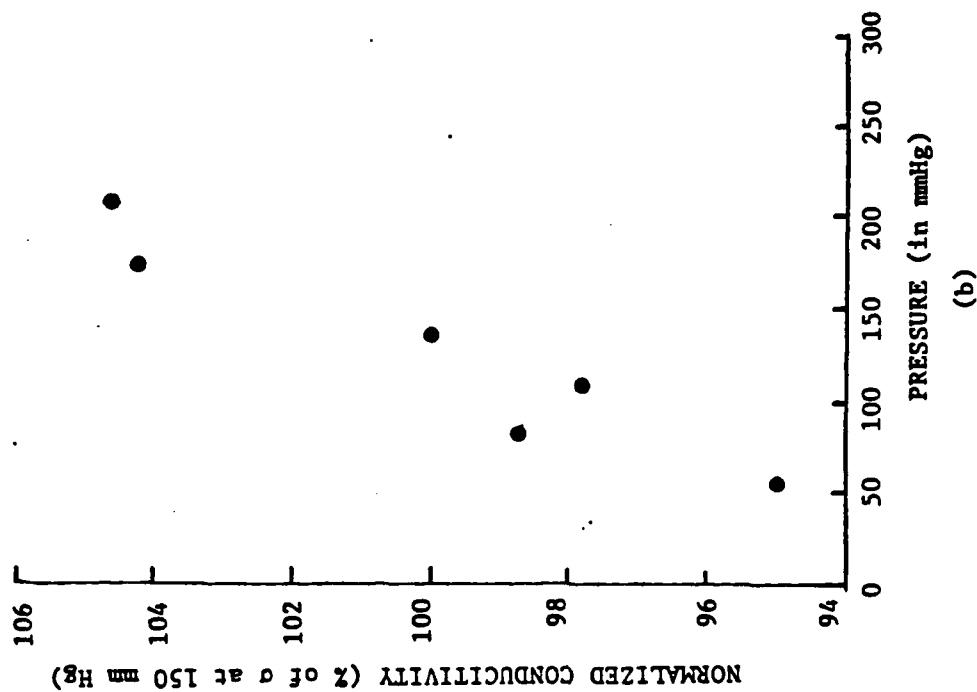
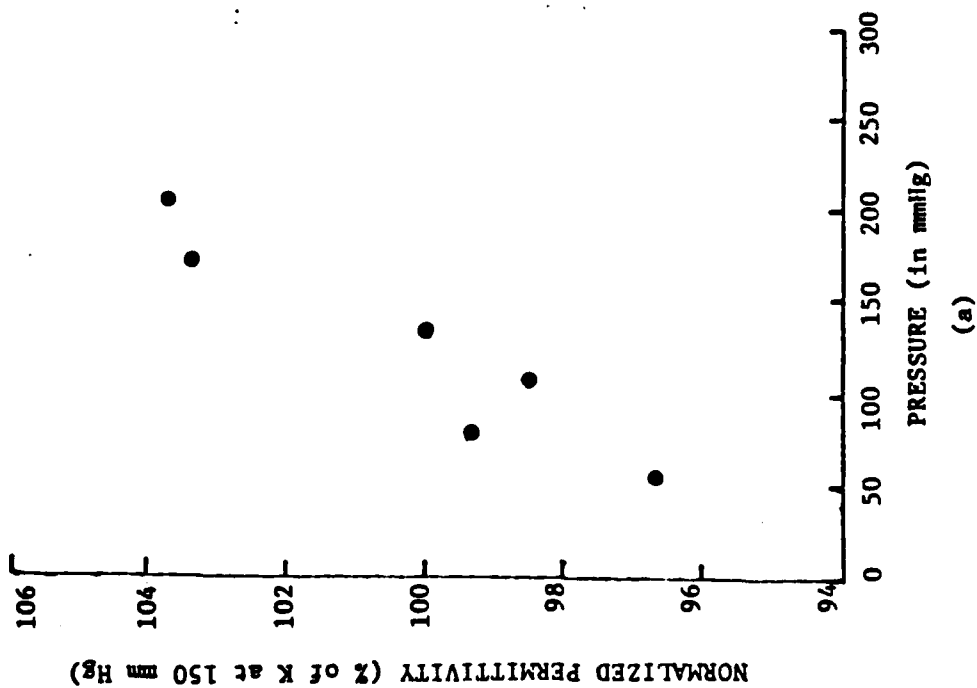


Figure 4. (a) Normalized permittivity, K, and (b) normalized conductivity, σ , as a function of pressure for a second typical isolated kidney perfusion experiment.

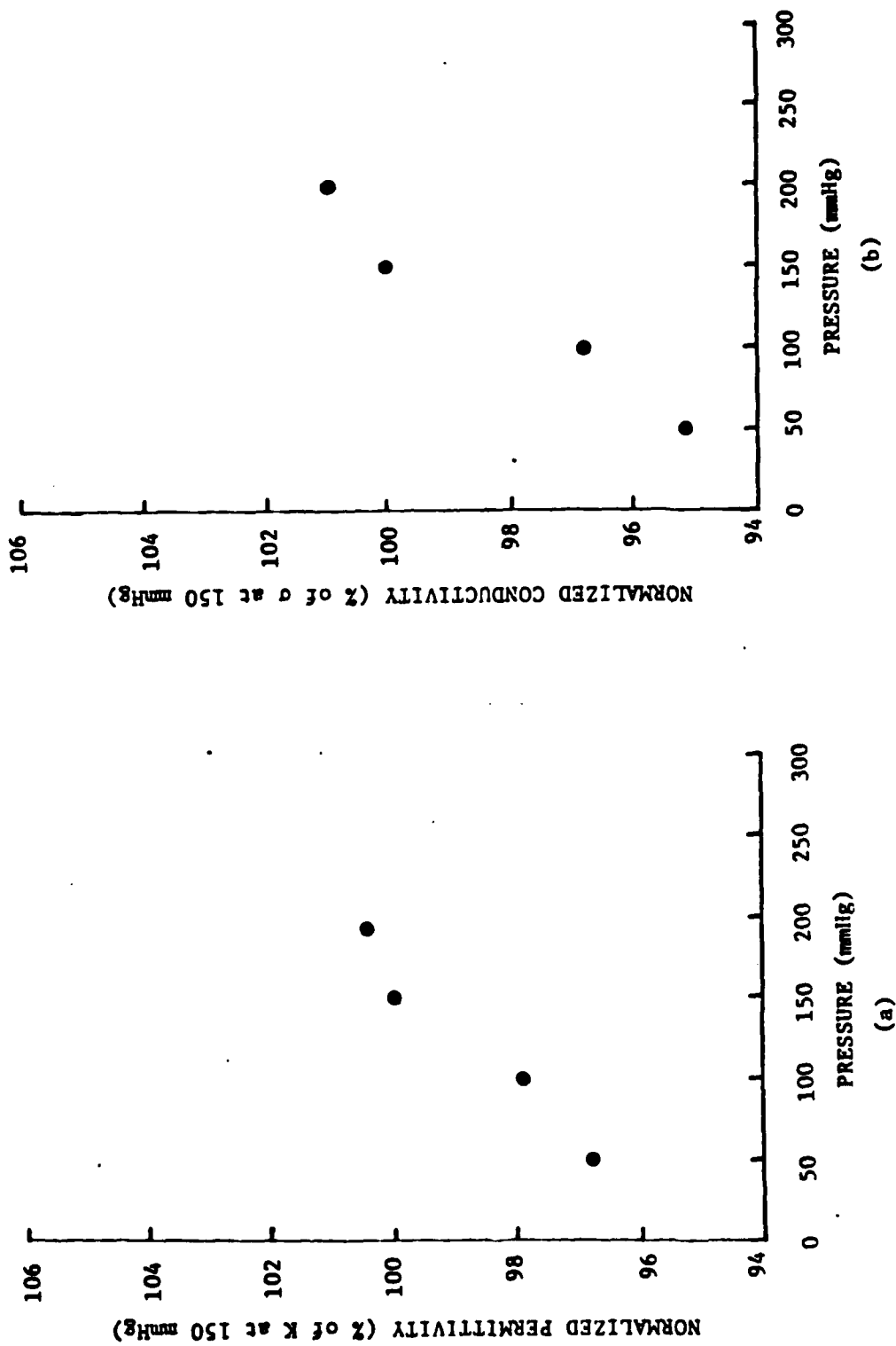


Figure 3. (a) Normalized permittivity, K , and (b) normalized conductivity, σ , as a function of pressure for one typical isolated kidney perfusion experiment.

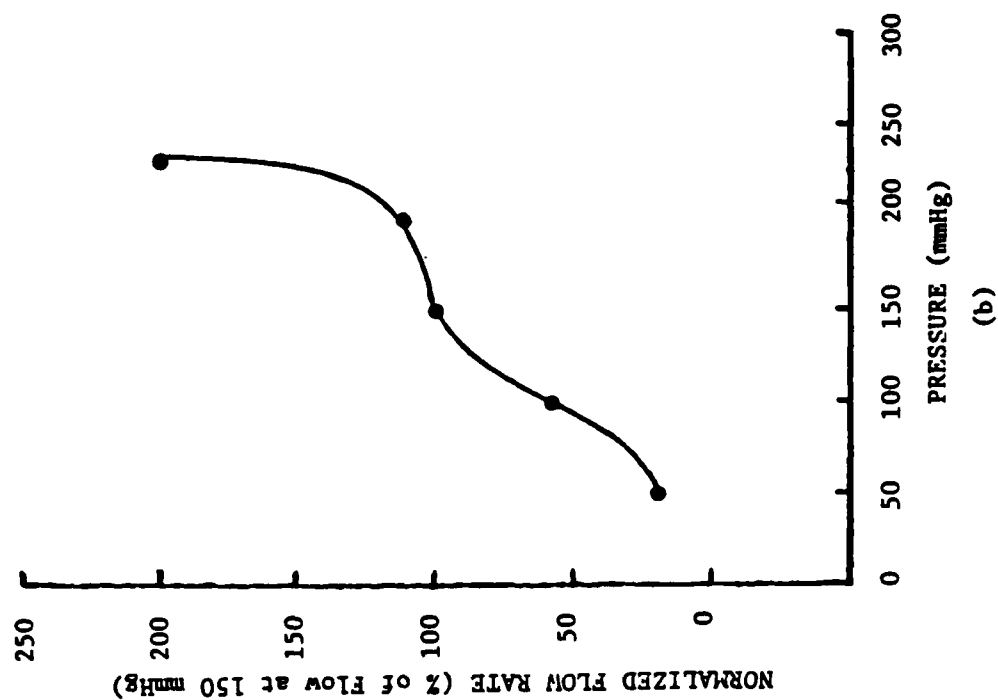
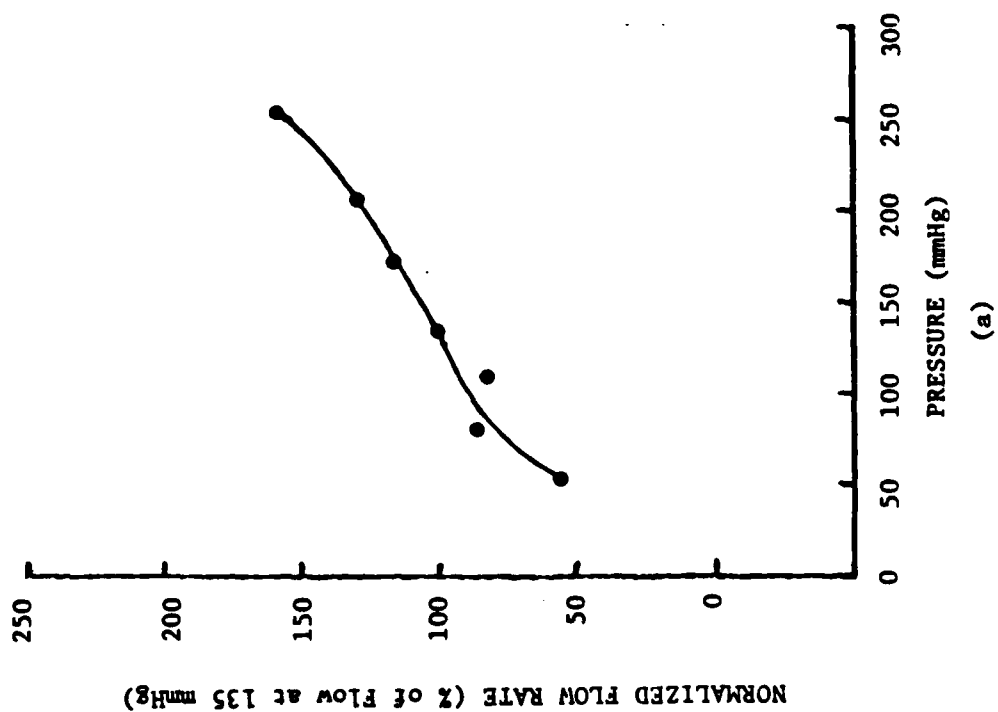


Figure 2. Normalized flow rate as a function of perfusion pressure for two separate kidneys.

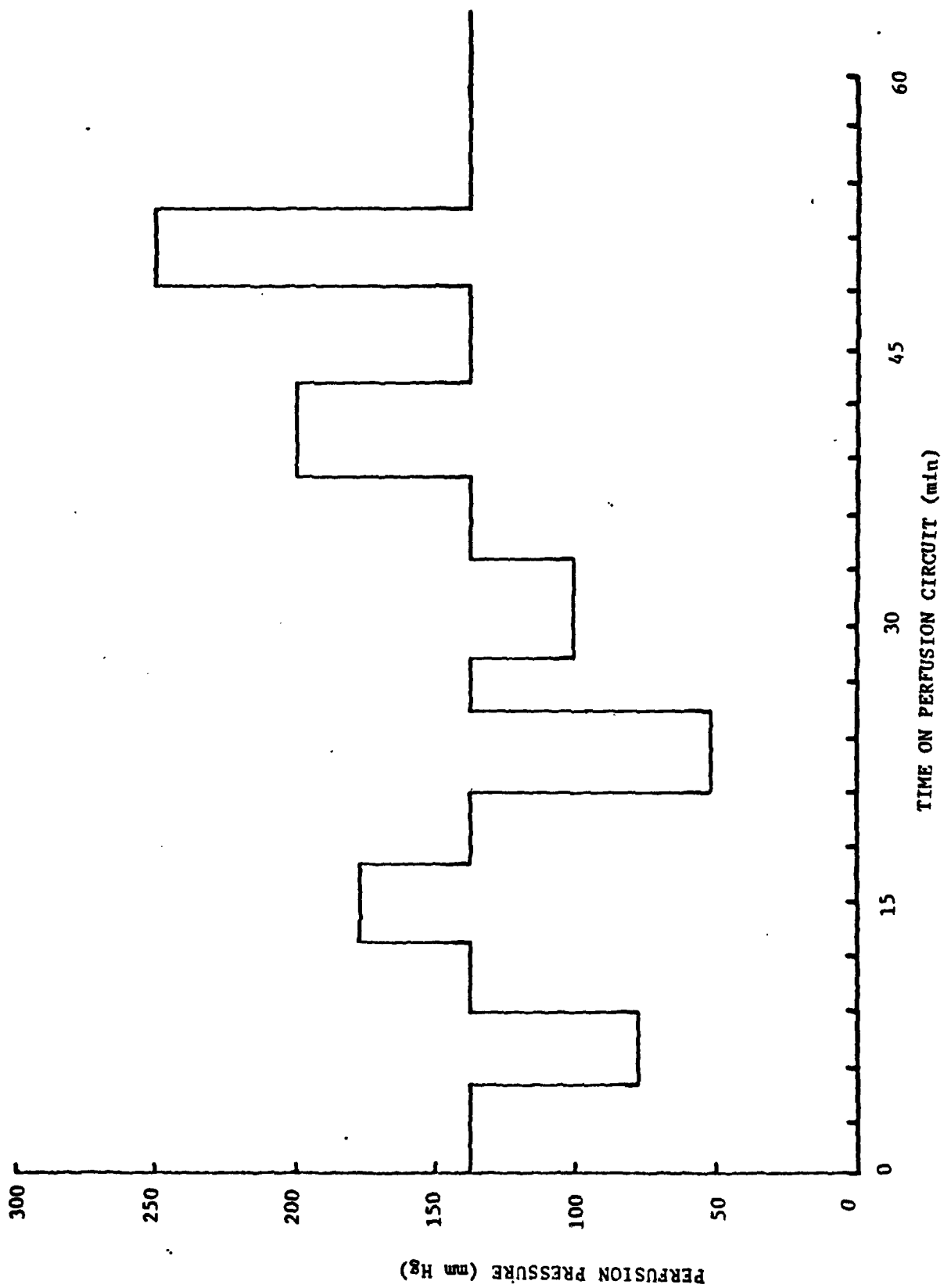


Figure 1. Perfusion pressure control regimen used for isolated perfused kidney experiments.

Efforts were also directed toward upgrading the perfusion circuit with all new tubing, and connectors of uniform 1/4-inch ID and with new larger-bore stopcocks. These changes were made consistent with plans for routine sterilization and to ensure uniform and minimum resistance in the perfusion circuit.

During the past year of this research program, additional numerical processing algorithms were written for data processing and analysis of parameters measured and stored during laboratory experiments. Modifications to existing algorithms were also made to permit parametric analysis of time-dependent changes in renal blood flow and complex permittivity, while accounting for and removing temperature-dependent effects. These algorithms were particularly useful in examining time-dependent drug-induced effects on regional renal blood flow and corresponding renal dielectric characteristics.

During the past year of the program, the following experiments were performed: (1) examination of regional renal dielectric property, perfusate flow, and glomerular filtration rate (GFR) changes as a function of perfusion pressure, (2) measurement of renal hemodynamic and dielectric changes during sympathetic nerve stimulation, and (3) examination of effects of known pharmacological adrenergic blockers on overall renal hemodynamics and cortical dielectric properties.

Animals were prepared and surgery was performed as described in previous quarterly technical reports and in Annual Report dated September 1982. Dog kidneys were isolated and perfused with a modified Krebs-Henseleit solution (including 5.7 mM Ca^{++} and 20g/l Bovine Serum Albumin). Following stabilization of the preparation, renal hemodynamic and dielectric characteristics were measured at different perfusion pressures. The baseline pressure used for normalization was 150 mm Hg or 135 mm Hg and perfusion pressure was varied from 50 mm Hg to 250 mm Hg using the regimen shown in Figure 1, where perfusion pressure is returned to baseline between each test pressure setting. Examples of the pressure-flow relationship and GFR changes typically observed are shown in Figure 2. The corresponding percentage changes in dielectric constant and conductivity are shown in Figures 3 and 4. The correlation of renal perfusate flow (RPF) rate with renal dielectric properties from the examples of Figures 3 and 4 is presented in Figures 5 and 6. In each case, very good correlation between changes in RPF and dielectric properties was observed. As in results previously reported, cases where flow was autoregulated exhibited dielectric constant and conductivity changes which corresponded directly with RPF autoregulation.

drain the venous effluent. It was necessary to collect samples of both urine and venous outflow in order to calculate creatinine clearance and GFR for small urine volumes. Urine was collected in preweighed vials over a timed interval and the urine volume was determined gravimetrically. We are currently investigating the relative cost-effectiveness and ease of measuring inulin concentrations by standard chemical analyses as opposed to scintillation counting methods using radio-labelled inulin. Of the costs for chemical analysis are comparable to those for creatinine, inulin clearance will also be measured in selected experiments.

Efforts to improve our perfusion system and perfusate solution were continued through further review and evaluation of relevant published literature. An article by H. J. Schurek, et. al., (1975) [13] advocating the need for sterile, pyrogen-free solutions filtered through 0.22 μ m (micropore) filters was obtained. Although more recent articles have debated the necessity of this degree of sterilization, Schurek presented impressive results demonstrating stabilization of flow rates in isolated kidneys for periods up to 4 hours. It was decided that Schurek's results were significant enough to warrant converting from the current 1.0 μ m gravity filtration system to a 0.2 μ m Millipore vacuum filtration system in an effort to make the renal blood flow in the isolated, perfused kidney more time-independent and stable. Also, steps were taken to make certain that all instruments, tubing, and components of our perfusion circuit were sterilized between experiments in an effort to obtain a pyrogen-free perfusion system. A Fisher Scientific in-line flowmeter with an expanded measurement range and more accurate scale was purchased and the new flowmeter was incorporated into the perfusion system to provide more accurate measurements of flow rate.

Additional changes in experimental technique were introduced in an attempt to minimize the trauma to the kidney during the nephrectomy and isolation. Prior to isolating the kidneys, the laboratory animal was heparinized with 5 mg/kg IV Heparin (2000 units/ml). Upon cannulation of the renal artery, the kidney was immediately flushed with sterile D₅NS solution with heparin, 1 unit/cc, and vasodilan, 1 ampule/l. Immediately following connection to the perfusion circuit, this initial flushing solution (together with the heparin and vasodilan) was flushed out and normal kidney function returned within 15 minutes following initiation of perfusion with our modified Krebs-Henseleit solution.

SECTION III
RESEARCH EFFORTS DURING THE PERIOD 1 OCTOBER 1982
THROUGH 31 DECEMBER 1982

The primary goal for the period 1 October 1982 through 31 December 1983 was to further establish the correlation between tissue dielectric properties and functional physiological changes. The question of physiological relevance to dielectric property changes was further examined through investigation (1) of neural and pharmacological influences on renal blood flow and in turn, on renal dielectric properties and (2) of changes in renal tubular absorption and secretion, and therefore, tubular flow, on medullary dielectric properties.

In an effort to further improve the in-vitro canine kidney model for studies of autoregulation and regional flow changes described in Annual Report dated September 1982 [12], certain changes were made in the surgical exposure of each kidney from an ipsilateral flank incision rather than a midline abdominal incision as was used in previous years, (2) cannulation of not only the renal artery, but also the ureter and possibly the renal vein, (3) improvements of the sterility of the perfusate and the perfusate filtration system, (4) pre-nephrectomy heparinization of the experimental animal and post-nephrectomy administration of heparin and vasodilan for the kidney, and (5) modifications of the perfusion circuit itself.

The change in surgical procedure to a flank incision approach to the kidney was made because of the need to improve accessibility of renal vessels and to shorten the duration of the surgical procedure. This surgical maneuver was used to approach kidneys during the last experimental series in the fourth year and in all experiments performed during the current research effort. The procedure was found to be quicker and less traumatic to both the dog and the kidney than procedures used previously. Because the kidney was accessible without having to enter the peritoneum and reach into the abdominal cavity, we found it much easier to isolate and cannulate.

During this year's studies, the ureter was cannulated in addition to the renal artery. This permitted monitoring the rate of urine production and insulin clearance. Glomerular filtration rate (GFR) was determined from the renal clearance of creatinine. Cannulation of the renal vein was not necessary because the organ chamber currently used is already designed to

probe holder, and (6) comparison of radioactive tracer and dielectric probe measurement results.

The procedure for measuring dielectric properties of renal tissue was outlined in Annual Report dated September 1982 [12]. The kidneys were surgically removed and placed on an in-vitro perfusion circuit. Care was taken to minimize the time between cessation of the normal blood flow and initiation of in-vitro perfusion. In most cases, this time was less than two minutes, and the greatest interval was five minutes. Following stabilization of the isolated kidney preparation, the renal dielectric properties were measured using the probe dielectric measurement technique. The dielectric properties were measured under varying controlled conditions of flow rate and arterial pressure.

Results of the in-vitro renal studies consistently showed a proportional relationship between renal flow and relative permittivity and conductivity. For cortex and medulla tissue types, autoregulation of renal flow was observed and the dielectric properties followed the same relationship. Both tissues exhibited dielectric changes in the same direction, although cortical changes were generally greater.

The data acquisition and logging system was upgraded to include 15 channels of signal-conditioning buffer amplifiers and a 10-position event marker, from which the output signals are routed through a multiplexing A/D converter capable of a 20 kHz sampling rate and to a Zenith/Heath WH-89 microcomputer having 300 kbytes disk storage. Software was developed during the fourth year research efforts to allow the WH-89 microcomputer to control the network analyzer system and overall data acquisition and to provide initial processing of measured data. New software was also written for multiplexing dielectric measurements data from up to five probes to permit simultaneous data recording at different measurement sites.

Programs developed on the Cyber 70/74 computer system were used to perform most data processing functions, including baseline subtraction, averaging, and computation of linear correlation coefficients and correlation probabilities for pairs of variables. These programs were used for the analysis of the measured renal physiological and dielectric property data.

In-situ dielectric measurements were performed over a two-hour period. Both dielectric property data and physiological data were recorded for 30 minutes prior to sacrificing the animal. This ensured physiological stability of the animal and permitted recording in-situ dielectric data under conditions of homeostasis. Sacrifice was performed by injecting a 20 cc bolus of saturated KCl or CaCl_2 into the femoral vein. All dielectric and physiological parameters were monitored for 90 minutes postmortem, with death being defined to be the time at which all systemic pressures were zero. A comparison of results obtained with KCl to those obtained with CaCl_2 sacrifice can be found in Tables II and II in Section III of Annual Report dated September 1980 [10]. The overall trend in both groups is similar. Both conductivity and dielectric constant gradually decrease as a function of time postmortem. However, in cases of CaCl_2 sacrifice, the values peak immediately upon intravenous injection and change more than in the KCl cases. While nominal values for the dielectric constant are about 57 in both cases, the CaCl_2 sacrifice results in an increase to about 62.3, or a change of approximately 10%. This peak occurs from 6-10 seconds before systemic pressures reach zero. This indicates that the CaCl_2 injection causes a stronger and more abrupt change in blood flow to the brain, as would be expected from the different mechanisms by which the K^+ and Ca^{2+} ions cause death.

Studies of the effects of changing renal blood flow on the dielectric properties of kidney cortex and medulla were also performed. A decrease in total renal flow consistently produced a decrease in both relative dielectric constant and conductivity, and an increased renal flow resulted in an increase in the properties. Measurements on renal tissue were performed both in-situ in living dogs and in-vitro using isolated, perfused kidneys. Measured renal dielectric changes were observed to follow kidney autoregulatory behavior.

During the fourth year of the program, the research investigations performed included (1) dielectric measurements of renal tissue under controlled perfusion conditions, (2) investigations of different artificial perfusate solutions to develop a solution which best preserved renal function, (3) characterization of renal pressure-flow relationships using both in-line flow measurement and radioactive tracer techniques, (4) design and development of software for a fully automated data acquisition and processing system, (5) development of a controlled contact force multiple

stabilized by decreasing the in-line variable resistance in the perfusion circuit (thus increasing RPP). Table 1 shows the renal vascular and dielectric responses to alpha adrenegic receptor antagonism with phentolamine. RPP was maintained at 150 ± 5 mm Hg and RPF, GFR, and dielectric properties were recorded. RPF increased 25% from baseline control values with the infusion of 35 mg of phentolamine into the renal perfusion circuit. GFR increased an average of 40% within 10 minutes thereafter. Increases in both relative dielectric constant and conductivity were measured which were proportional to the measured vascular changes. The relative dielectric constant increased approximately 4.5% and the conductivity increased approximately 5% from control values following stabilization of vascular parameters. These results again indicate that the effects of vasoactive drugs can be examined from measured dielectric property changes using the probe technique.

TABLE 1
RENAL VASCULAR AND DIELECTRIC RESPONSES TO ADMINISTRATION OF REGITINE
(n=3)

	Renal Perfusion Pressure (mm Hg)	Renal Perfusate Flow (% of flow @ 150 mm)	Dielectric Constant (% from baseline)	Conductivity (% from baseline)
Prior to Regitine Administration	150 ± 3	0	0	0
5 min. after	150 ± 5	8	-0.1	-0.2
10 min. after	150 ± 4	12	-0.1	-0.2
20 min. after	150 ± 6	16	2.6	2.5
30 min. after	150 ± 3	21	3.7	4.3
40 min. after	150 ± 3	20	4.7	5.0

SECTION IV

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