

# FluidSim3 (v80) manual

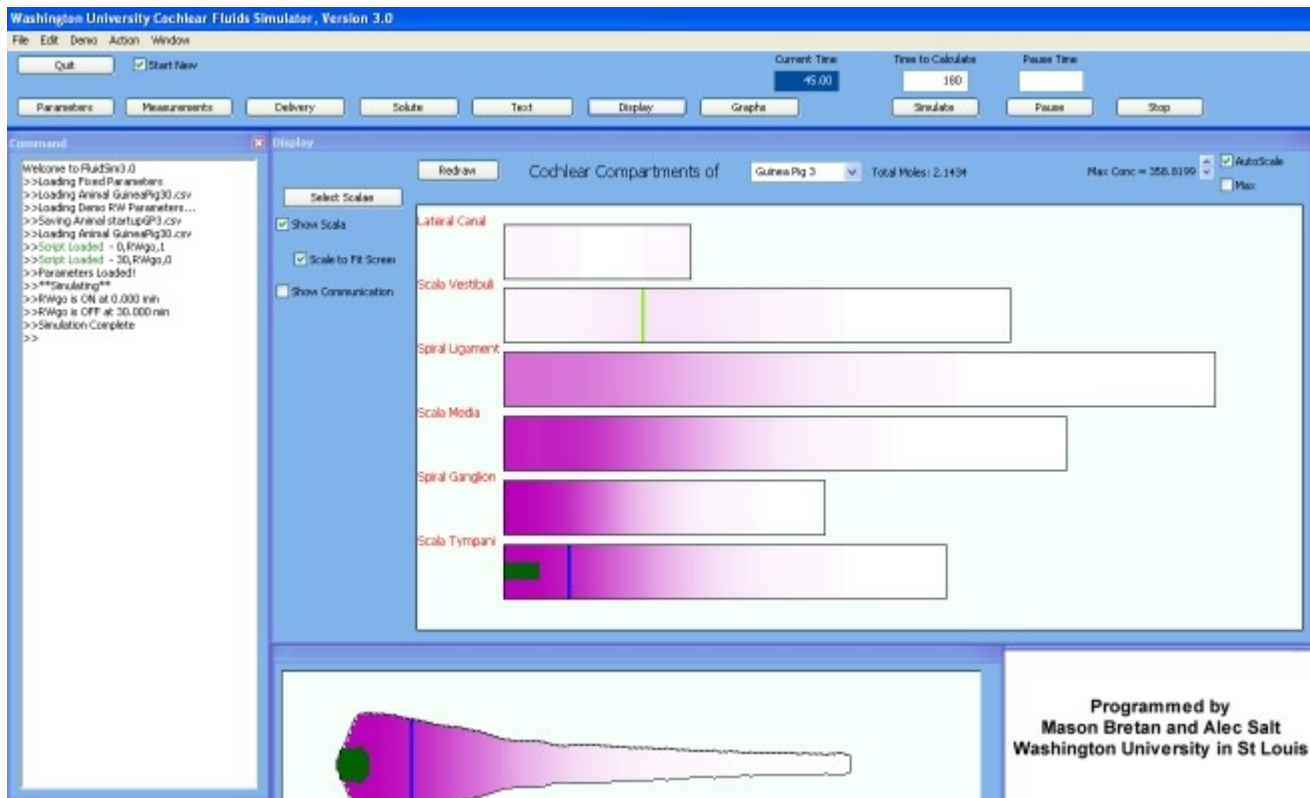
Alec N. Salt, Ph.D.

Department of Otolaryngology

Washington University School of Medicine

St Louis, MO, 63110, USA

Current program revision 3.080, February 2012



## Overview

This computer program **simulates the movements of drugs and other solutes in the fluid spaces of the inner ear under different experimental conditions**. It is intended for use by researchers and clinicians who are applying drugs or other substances to the inner ear. It is not intended as “entertainment”, unless you have an odd taste in entertainment.

Drug distributions can be calculated for a variety of common delivery procedures, and for fluids sampling and measurement methods that are commonly used experimentally. The program does not find “a solution to fit your data”. At present, it only determines the drug distribution (concentrations at specific locations, sample measurements, etc) for a set of parameters that you provide.

The choice of parameters for different substances under different conditions remains a “work in progress”. More parameters will be made available as we demonstrate their ability to represent experimental data. At present the model is being made available “as is”. Be aware that there are many parameters that can dramatically influence results and inappropriate settings can represent “non-physiologic” situations.

## Installation

### Windows PCs

Download the simulator program for Windows (5.4 mB Zip file)

Save the Zip file to your desktop, then right click on it and “Extract” the contents.

This will create the FluidSim3 folder at a location you choose (default=wherever you saved the zip file).

If you click on the folder to open it, you can then click on Fluidsim3.exe which will start the program. You can also right-click on the program icon, drag it to the desktop and select “Create shortcut” so that a program icon is placed on the desktop.

Do not move the program itself. The entire folder can be moved but the program must remain in the Fluidsim3 folder with all the associated files (including the library folder) in order to run.

You may wish to make a copy of all the setup (\*.csv) files. If these files get corrupted in some way, the program may not run.

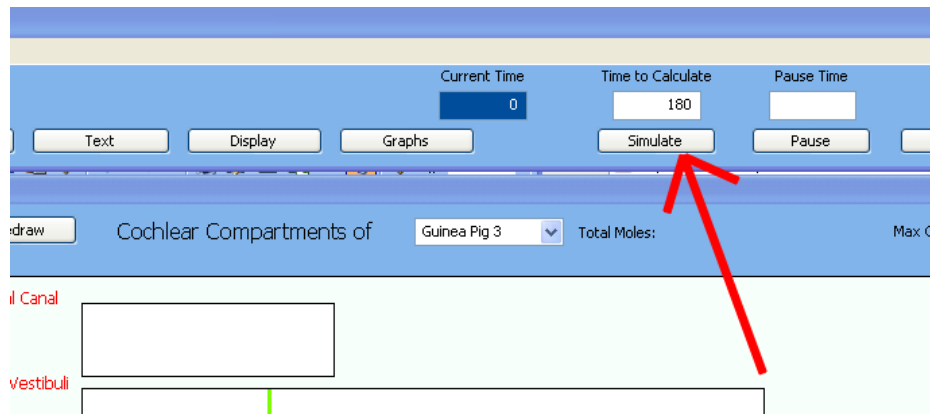
### Mac (It runs faster on a Mac ☺)

Download the simulator program for MAC (3.4 mB Zip file). Usually it will be in your “Downloads” directory. Drag the Fluidsim3 folder to your desktop, your Documents directory, or to the applications folder. Wherever you like. In this folder click the Fluidsim3 file to start the program

A shortcut to the FluidSim3 app can be dragged to the dock to make it easier to start.

### Initial Trial Run

When the simulator is loaded, try hitting the “Simulate” button. A simulation should start running, using pre-set parameters. If it doesn’t, make sure the application program is in the folder with all the library files before sending me an e-mail at [salta@ent.wustl.edu](mailto:salta@ent.wustl.edu).



You may also want to try the 4 “Demos” from the program bar at the top. If these programs don’t run, you will need to contact me.

**Some of the screen may look a little different from this manual. I'll try to update the manual when I have time**

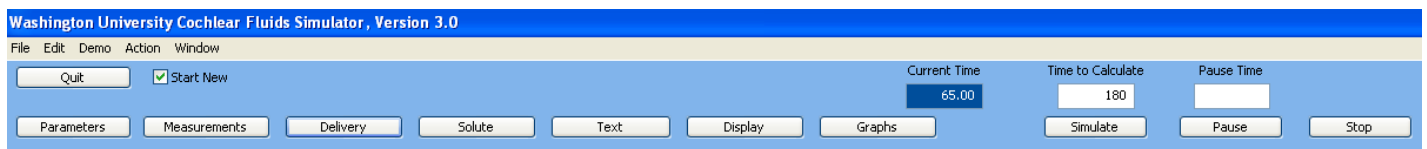
## Changes relative to prior versions of the simulator

The prior program made available on the internet (Fluidsim 1.6, written in Microsoft Visual Basic) was based on the 3 fluid spaces of the cochlea as shown in the table. In many types of experiments, it became apparent that substances applied to the ear do not stay confined to the fluids in the scalae, but instead distribute into all the tissues and other compartments of the ear. The new program, Fluidsim 3.0, now incorporates all the major fluid and tissue filled compartments of the both the cochlea and vestibular systems.

Fluidsim 1.6	Fluidsim 3.0
Scala Tympani	Scala Tympani
Scala Media	Organ of Corti
Scala Vestibuli	Endolymphatic Space
Compartment “parallel to scala tympani”	Scala Vestibuli + Vestibule
	Spiral Ligament
	Spiral Ganglion
	Auditory Nerve
	Lateral Semi-circular canal (endolymph and perilymph)
	Posterior Semi-circular canal (endolymph and perilymph)
	Anterior Semi-circular canal (endolymph and perilymph)
	Sacculle, Utricle (endolymph)

A result of increasing the number of compartments is that the number of parameters has increased. However, many parameters can be “grouped” and some others (nonexistent processes) can be ignored for most purposes. Solutions can often be obtained by adjusting a limited number of parameters.

## The Control Bar



This is the main control of the program. Each of the 7 buttons at the lower left opens a specific window, each of which is presented below.

The “Simulate”, “Pause”, “Stop” control the calculations of the simulator. Note that parameter changes cannot be made while calculating, but are only made while stopped or paused. All parameters are re-read on restart.

“Quit” closes the program saving the current configuration. Unlike the prior simulator, all parameters used for specific calculations can be stored and recalled as required.

Close the control bar window (With red Windows X, or red button on Mac) to stop the program without saving the current setup.

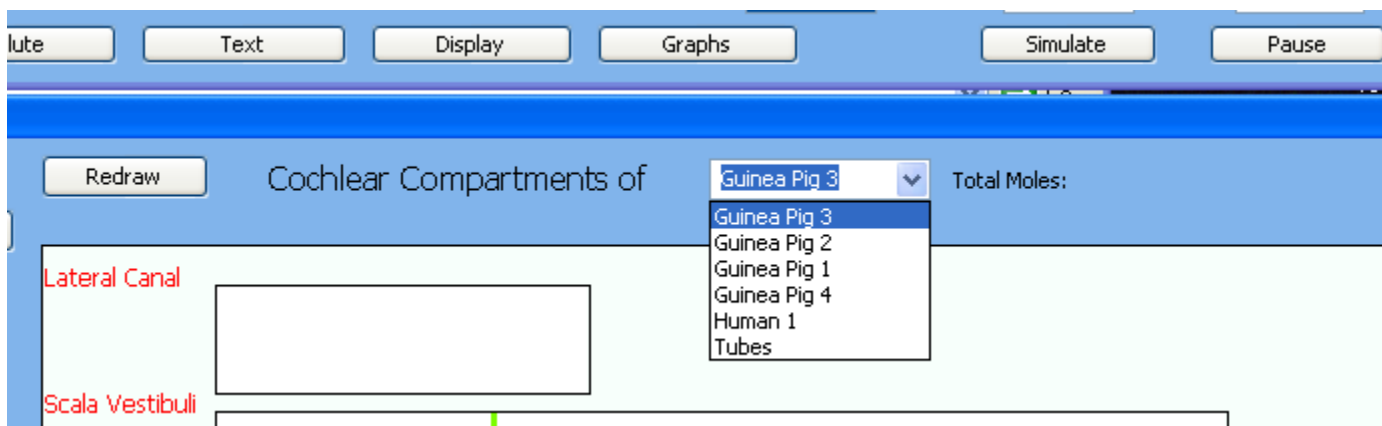
## Species that the Model will Simulate

This version of the model primarily simulates the **guinea pig and the human cochlea**.

There is no reason why the dimensions of other species cannot be added to the simulator. The limitation is the availability of 3D data sets from which dimensions of each fluid and tissue compartment can be derived.

If you have an interest in performing calculations in other species, I would encourage you to help generate the required data for the dimensions of the ear for that species. I'll be happy to work with you to add the data to the program.

### Current options are :



**Guinea pig 3 :** Version 3 of the guinea pig, with all fluid and tissue compartments of the ear specified.

**Guinea Pig 2 :** Provides compatibility/comparisons with Fluidsim 2.0 (which was not made available on the web but includes the vestibule)

**Guinea Pig 1 :** Provides compatibility/comparisons with Fluidsim 1.6 (last internet version)

**Guinea pig 4 :** is currently for debugging purposes. It has uniform CSA with distance and uniform interconnections between adjacent compartment.

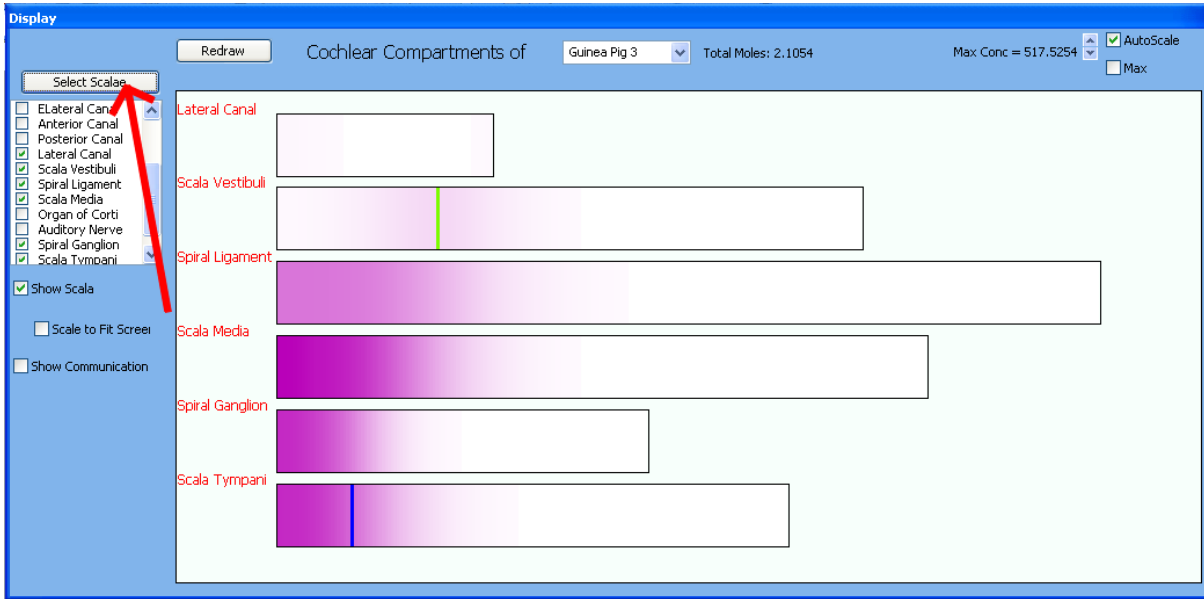
**Human 1:** Uses the old simple 3-compartment data for humans that was available in Fluidsim 1.6.

**Human 2 :** Uses the new human data. This includes the cochlear tissues and spaces, but only part of the vestibule and SCC. We are still working on these data.

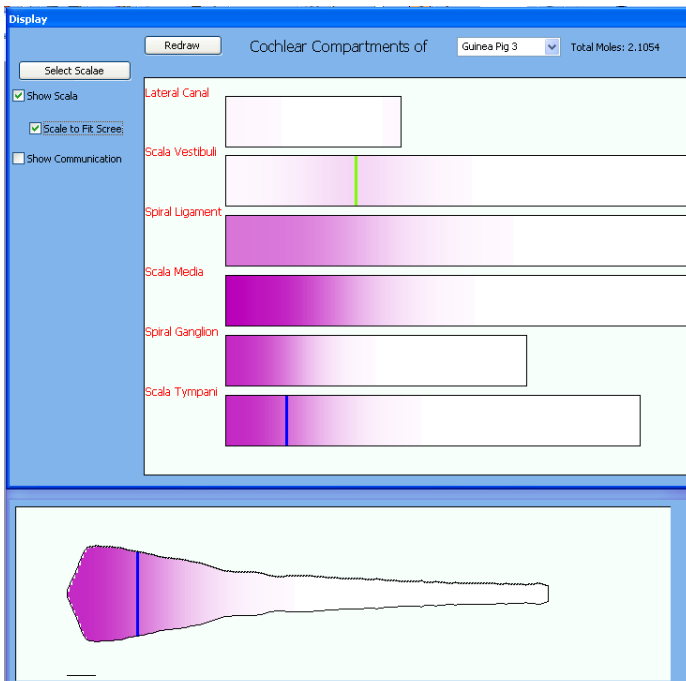
**Tubes:** Simple straight tubes so that flow/communication algorithms can be validated.

## The “Display” Page : Compartment areas and Communications

Compartment areas are defined in spreadsheets (For Guinea pig 3, the source file is GuineaPig30.csv). The interconnections between compartments are defined in a second file, GuineaPig30Transfer.csv. Both scala area and interscala communications can be viewed on the “Display” page

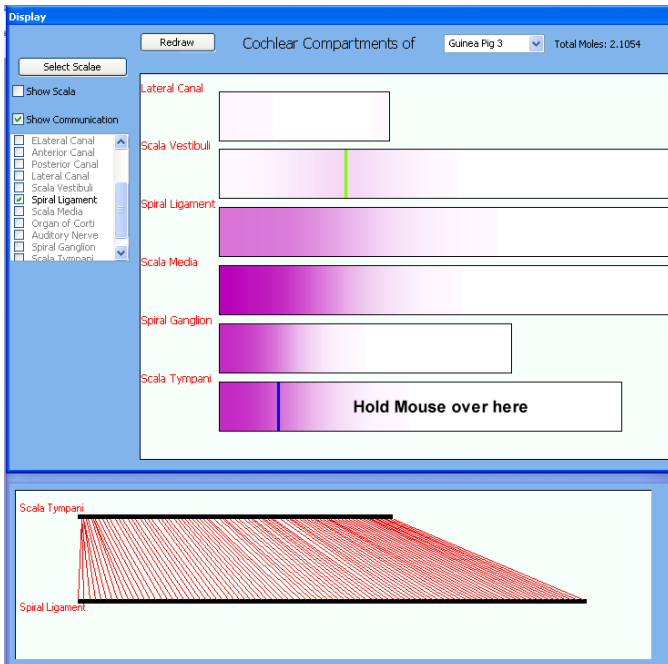


The Display page allows you to view concentration profiles with distance in up to 6 compartments, selected by the “Select Scalae” button (Red arrow). Note that the choice of compartments that are viewed does NOT affect the calculations, which always involves all available compartments. When you have selected all 6, the others become grayed out and unavailable. So, if you are having trouble adding a compartment, then turn one or more of the selected compartments off.



If the “Show scala” option is checked, then rolling the mouse cursor over a displayed tube representing a compartment will pop up another window that shows the corresponding scala with anatomically-correct cross section.

This is useful to understand how results depend on scala area, but having this window open carries an overhead and may result in slower calculations. The window can be closed by moving the mouse cursor off of the display page or by unchecking the “Show Scala” box on the left.

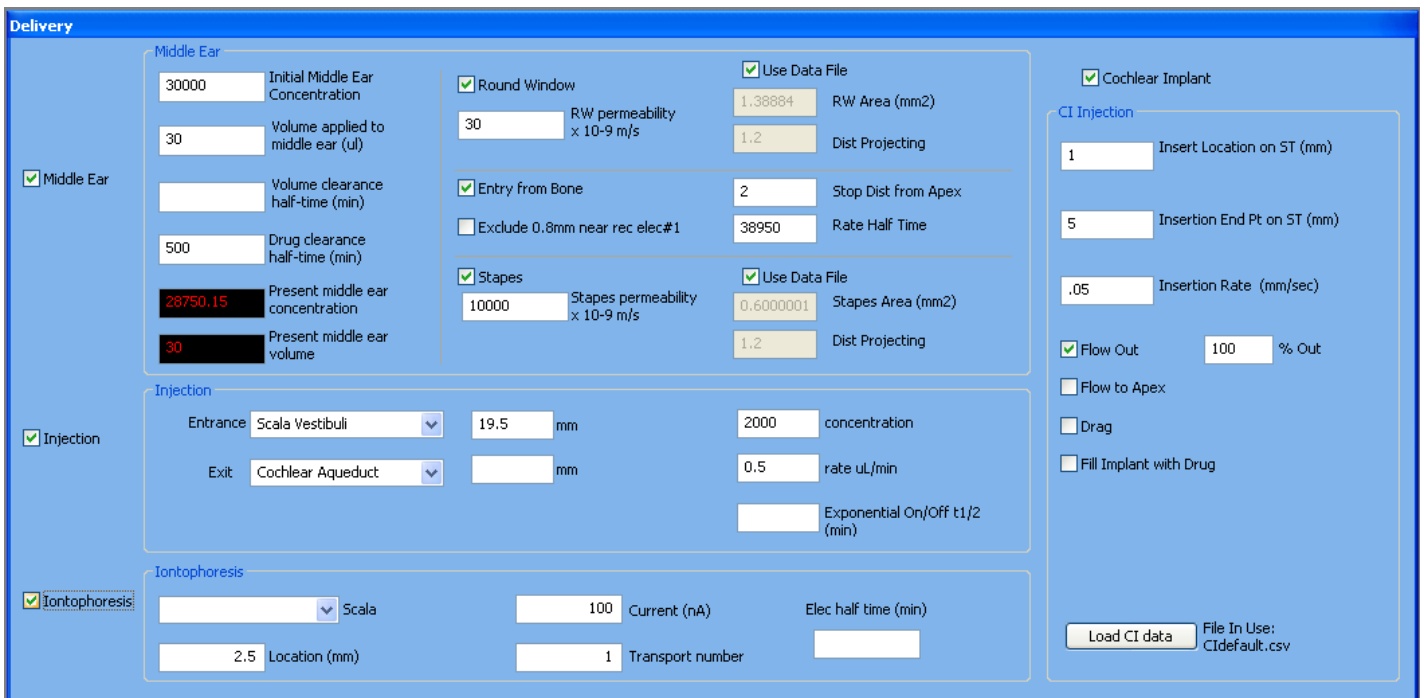


The “Show Communications” option changes the view of the scala window so that “interconnections” between parallel fluid/tissue compartments are shown.

In this example the “spiral ligament” is selected as the reference compartment. When the mouse is held over compartments which lie adjacent to the spiral ligament, the defined alignments of the two compartments (often of different length) are shown graphically. So, holding the mouse over scala tympani shows how the shorter scala tympani communicates with the longer spiral ligament over the length of both structures.

The panel shows how solutes in specific regions of each compartment interact with those adjacent. The data are anatomically-based and have been derived from 3D reconstructions of the ear.

### The “Delivery” Page: Processes that apply drugs locally to the ear



The “Middle Ear” option allows Intratympanic applications to be simulated

An initial concentration and applied volume is set, together with potential sources of loss of drug from the middle ear, such as from volume loss (Volume Clearance half time) or from clearance by the mucosa (Drug

clearance half time). The effects of middle ear clearances are shown in the boxes with red text (not set by the user) and can be saved or shown graphically on other pages.

Entry from the middle ear to the inner ear is defined by 3 routes.

- 1) Entry through the RW membrane, defined by a permeability value.
- 2) Entry into perilymph at the apex through the bony otic capsule. This is defined by a half time of entry into SV, ST and SL for an apical region reaching a specified distance down the cochlea.
- 3) Entry into SV via the stapes footplate, defined by a permeability value.

**The Injection option** allows volume injections, perfusions, etc to be simulated

The injection and exit points are defined, together with the applied concentration and the injection rate. While the injection is on, volume flow between the injection and exit sites at the specified rate is simulated. Be aware that for a specific injection rate the linear rate of flow along the scala will depend on the cross-section of the scala, being faster in apical regions of lower cross-section, and slower in basal regions with larger cross-section.

In reality, some injection pumps do not start or stop instantly (if they have compliant coupling tubes). To accommodate this, an onset and off half time can be set, which causes the flow rate to increase and decrease exponentially at the onset and finish.

**The Iontophoresis option** allows a current-driven iontophoresis to be simulated, allowing drug applications without volume disturbance to occur. The polarity of current is assumed to be that which causes ejection of the ion, from the application pipette to the scala. The transport number represents the proportion of the applied current that is carried by the drug being injected.

**The Cochlear Implant option** allows a number of types of drug application associated with cochlear implantation to be simulated. This includes:

- 1) Ability to define cochlear implant dimensions and insertion depth
- 2) Automatic adjustment of remaining scala tympani cross sectional area as the implant is inserted,
- 3) Displacement of perilymph and drug in ST towards the cochleostomy site during insertion.
- 4) Displacement of fluid and drug in ST towards apex during insertion (not proven to occur)
- 5) Apically-directed drag of fluid around the implant towards the apex during insertion.
- 6) Drug elution from the implant

## The “Measurements” Page :

**Measurements**

**Point Measurements** Interval(sec) 60

	Scala	Location(mm)	Concentration	Volume
<input checked="" type="checkbox"/> Point #1	Scala Tympani	2.45	404.2503	
<input checked="" type="checkbox"/> Point #2	Scala Vestibuli	5.35	83.4897	
<input type="checkbox"/> Range			0	0

**Sampling** Scala Location(mm)

Perilymph Aspiration

10

185.5  Sampling Start Time

80% Away from Ampulla

	Duration (sec)	Vol (uL)	Measured Conc	Start Time	Calculated Vol	Calculated Conc
1	138	2.116858238	931.1143505			
2	123.66...	2.102490421	975.6058266			
3	137.66...	2.131226054	900.552228			
4	131.33...	2.097701149	826.0380517			
5	139.33...	2.112068966	767.9847228			
6	131.66...	2.126436782	650.6568145			
7	134	2.092911877	515.7341654			
8	127	2.035440613	377.895074			

**Save 3D Data**

Compartment	Concentration	
Scala Tympani		<input type="checkbox"/>
Spiral Ganglion		<input type="checkbox"/>
Auditory Nerve		<input type="checkbox"/>
Organ of Corti		<input type="checkbox"/>
Scala Media		<input type="checkbox"/>

Dialysis On

Note: Injections, perilymph flow and perilymph leak are suspended during sampling

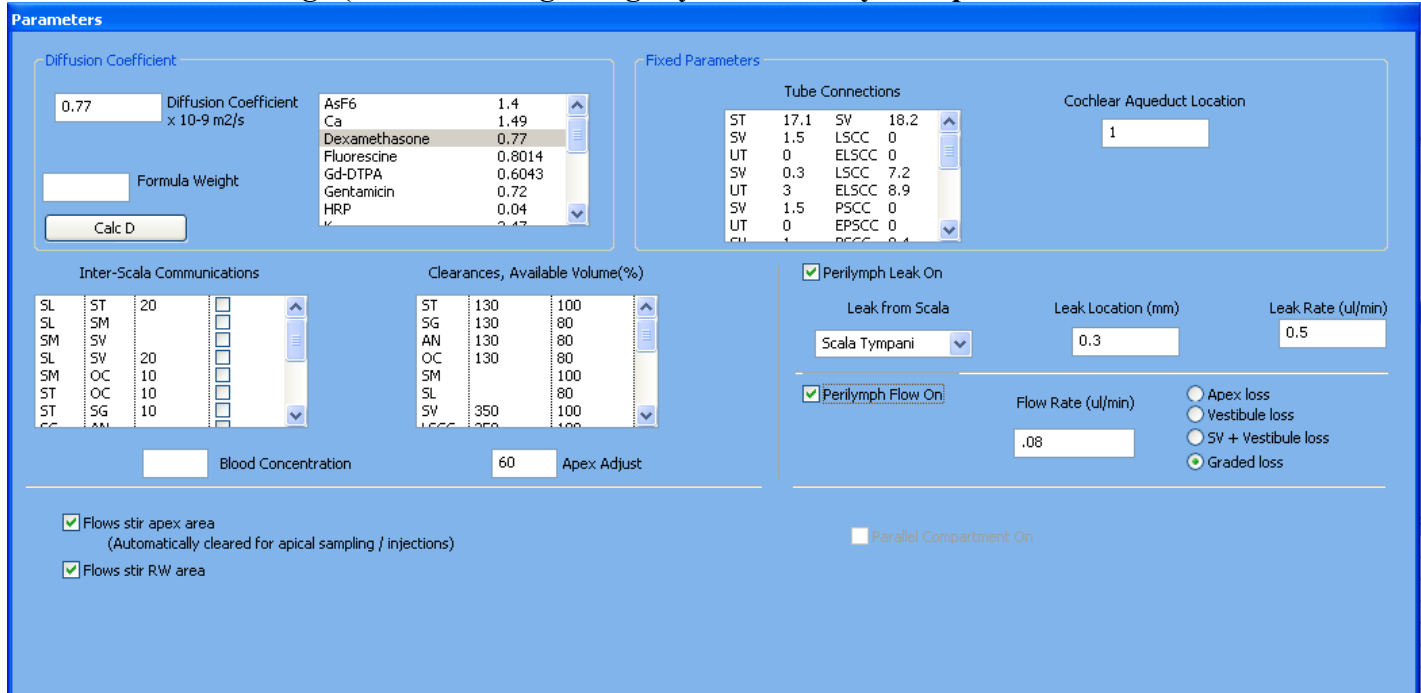
This page allows a number of types of measurement to be made including:

- 1) **Point measurements** at any location (simulates an ion-selective electrode at that location)
  - 2) **Range measurement**, similar to (1) except the measurement is made across a defined segment of the fluid spaces. This can represent a sample originating from the defined region.
  - 3) **Compartment measurements**, Measurements calculated for entire compartments, such as scala tympani or the spiral ligament, or for complete fluid spaces such as perilymph, endolymph, middle ear, etc.
- All of the above measurements can be graphed (See Graphs page) or time courses saved (see Text Page). In addition 3D data (concentration vs time and distance along a compartment) can be set to be saved here.
- 4) **Perilymph sampling**. This allows single or sequentially repeated samples with specified collection duration and volume to be simulated. Sampling takes into account the fluid flow within the cochlea that results from the sampling procedures,

To turn sampling on check the “Perilymph Aspiration” box and set the location at which you would like to sample. Then set the number of samples to be taken and time at which the sampling should start in the corresponding text boxes. In the seven column spreadsheet the “Duration” in seconds and the “Volume” in microliters must be defined. These refer to the duration of each individual sample and the volume of the sample collected in that time. These values can be entered manually but can also be loaded into the spreadsheet via a .csv file by pressing the “Load Sample File” button. This csv file should contain 3 columns

containing the numerical values of the duration(seconds), volume(uLiters), and concentration respectively for each measured sample.

**The “Parameters” Page (This has changed slightly – with “Easy Set” parameters for some substances.**



Parameters on this page define the characteristics of a drug or solute. Our goal is to eventually be able to select the substance and for appropriate parameters to be loaded. We have not yet reached that point. We are presently working to define parameters for TMPA (the marker ion we have used extensively), dexamethasone and fluorescein (which we are also using) that account for measured data. Some parameters may apply to all drugs (such as volume flow), some may be high specific to a drug and others may be similar for many drugs. This is an important part of our current research.

**Fixed parameters**

The tube connections at the upper right are defined in the “fixed parameters” (fixedparams.csv) file and cannot be edited here. The panel just provides details of the connections. For example on the top line it shows that ST at 17.1 mm from the base is connected to SV at 18.2 mm from the base (i.e. defining the communication for diffusion and flow at the helicotrema).

**Adjustable Parameters**

**1) Diffusion coefficient**

Some values for common drugs and solutes are provided. Selecting one transfers the appropriate value to the diffusion coefficient box. Values you use commonly can be added to this list by editing the fixedparameters.csv file. (Make sure you keep a backup copy before making any edits).

Also, the value of the diffusion coefficient can be entered in the box directly.

Thirdly, a diffusion coefficient can be estimated by entering the formula weight of the substance. Note that the counter-ions in the drug formula should not be included, as the ionized drug largely diffuses independently of the counter ions. So, for example, if the drug is disodium dexamethasone phosphate (a disodium salt) then the molecular weight of sodium, multiplied by 2, should be subtracted from the formula weight on the bottle.

## **2) Inter-Scala Communications**

All communications between adjacent compartments are defined in terms of the half-time of that process for the compartment in the left-hand column.

For example, the upper line sets up communication between the SL and ST with a half time of 20 mins in the SL. Note that due to both CSA and communication processes varying with location, the half time in ST will not be the same, and will vary with distance along the ear.

To make it more complex, for many compartments, the kinetics are likely not uniform with distance along the compartment and part of the challenge is to use algorithms that best represent the measured data. One option we have found useful (and is selected by the checkbox in this panel) is to normalize the communication so that the defined half time refers to the *average* cross-section of the compartment, but which causes parts of the compartment with smaller CSA to have more rapid kinetics and parts with larger CSA to have slower kinetics.

## **3) Clearances (Elimination) to blood.**

The half times (in mins) in column two define the rate that drug is lost from the ear to an “infinite pool”, representing the blood.

## **4) Available Volume (%)**

For tissue-filled compartments, such as the spiral ligament, the drug may not have access to the entire compartment volume, such as the intracellular spaces. This column allows the volume of a tissue-filled compartment to be adjusted to reflect this. This variable becomes important in trying to balance the loss of drug to a compartment during drug loading and the diffusion of drug back into the scala during fluid sampling procedures. 100 % indicates the entire compartment volume is available to the drug.

## **5) Blood concentration**

To simulate systemic application of drug, a blood level of drug can be defined. The ability to define a plasma timecourse of drug (possible with FluidSim 2.0) is not yet available in this version of the model.

## **6) Apex adjust**

Some data indicate that communication with blood (as defined by the half time within the compartment) occurs less readily in apical regions than at the base. This variable allows the elimination rate to blood of ST, SV and SL to be reduced in a graded fashion from base to apex. Entering 100 (%) here sets uniform communications along the compartment. Entering 60 (%) sets the apical elimination to be 60% of that of the base. The algorithm reduces the rate constant of the communication ( $\log(2)/\text{halftime}$ ) linearly from the base to a point 70% of the apical-basal distance. Communication in the apical region (30% of the distance) is uniform, at the defined amount (e.g. 60%) re. the base. Although this was set arbitrarily, it was defined this

way because the apical regions represent a very small part of the total volume and otherwise, very high gradients had to be established to see a perceptible difference.

### **7) Flow stirs apex / Flow stirs RW area options**

Anatomically, the cochlear aqueduct does not enter ST at the base, but about 1 mm from the base. Similarly, the ST does not enter SV at the end of SV, but enters a little before the end. For diffusion, these locations are important. But when calculating flows through the system it can leave “unstirred” regions that flow does not occur through. We think it is unlikely that such unstirred regions exist during flow, so this option has been added to allow calculations either way. In reality, these regions are extremely small, so it makes only minuscule differences to samples, measurements.

### **8) Perilymph Leak**

Perforations of the otic capsule immediately result in leaks driven by CSF pressure. This option allows leakage at a specified rate (typically about 1  $\mu\text{L}/\text{min}$ ) to be defined for specific location, with fluid being replaced by CSF entry at the aqueduct and volume flow through the scalae between the two locations.

### **9) Perilymph Flow**

Almost all of our ST measurement and sample data suggest that in the sealed cochlea, there is a very slow entry of CSF at the cochlear aqueduct, of about 10 – 30  $\text{nl}/\text{min}$ . The consequences for drug dilution in the basal turn of ST are very apparent, but the outlet for this volume, and whether the outlet is for fluid only, or fluid and drug, remains to be established. For example, when the bulla is open, there may be evaporation from the bone of the cochlea, replaced by CSF entry (at higher rates when the bulla is open), but there would not be loss of drug from the site of evaporation.

This algorithm therefore simulates CSF influx at a specified rate with a variety of options of where the outlet site is likely to be. The volume loss can occur at the apex, the vestibule, throughout the vestibule and ST. Finally, the flow may be graded throughout the entire system (from the base of ST to the base of SV) with flow rate declining uniformly. This latter option appears to best represent the data. Note that this causes solute movements associated with flows but there is no solute loss from the system with this algorithm.

## The “Solute” Page

Solute Entries			Amount in nMoles			Solute Losses		
Mid Ear	4.699	100.0%	Scala Tympani	0.530	11.3%	CSF	0.000	0.0%
Round Window	4.699	100.0%	Spiral Ganglion	0.018	0.4%	Blood	3.236	68.9%
Stapes	0.000	0.0%	Auditory Nerve	0.000	0.0%	Leak	0.000	0.0%
Injection Entry	0.000	0.0%	Organ of Corti	0.016	0.3%	Flow	0.000	0.0%
Blood	0.000	0.0%	Scala Media	0.000	0.0%	Sample	0.000	0.0%
Bone Entry	0.000	0.0%	Spiral Ligament	0.284	6.1%	Dialysis	0.000	0.0%
Iontophoresis	0.000	0.0%	Scala Vestibuli	0.524	11.1%	Injection Exit	0.000	0.0%
Initial CI	0.000	0.0%	Lateral Canal	0.017	0.4%	Mid Ear	0.000	0.0%
Leak	0.000	0.0%	Posterior Canal	0.039	0.8%	CI Entrance	0.000	0.0%
			Anterior Canal	0.015	0.3%	ST Blood	3.163	67.3%
			ELateral Canal	0.000	0.0%	SG Blood	0.037	0.8%
			EPosterior Canal	0.000	0.0%	AN Blood	0.000	0.0%
			EAnterior Canal	0.000	0.0%	OC Blood	0.036	0.8%
			Utricle	0.000	0.0%	SM Blood	0.000	0.0%
			Sacculle	0.000	0.0%	SL Blood	0.000	0.0%
			Ductus Reunians	0.000	0.0%	SV Blood	0.012	0.3%
						LSCC Blood	0.001	0.0%
						PSCC Blood	0.003	0.1%

The Solute Page gives a useful overview of where the drug has “gone” during a procedure.

It summarizes the total amount of drug entering (absolute and normalized) in the left block

It summarizes the amount of drug presently in each of the compartments of the ear (middle block)

It summarized the amount of solute lost to other compartments outside the ear.

## The “Text“ Page

Data Table

Measurement Data

Minutes	Point 1	Point 2	Scala Tympani	Scala Vestibuli
0	0	0	0	0
0.25	4.253702e-9	2.880402e-7	14.854	0.0009167
0.5	9.652038e-6	0.0000174	27.88626	0.0052148
0.75	0.0004735	0.000159	39.69106	0.0140177
1	0.0053632	0.0006929	50.5553	0.0278315
1.25	0.0288298	0.0020462	60.65246	0.0469318
1.5	0.1000904	0.0047712	70.10225	0.0714717
1.75	0.2625144	0.0095076	78.99397	0.1015272
2	0.5684623	0.0169498	87.39754	0.1371233
2.25	1.073054	0.0278196	95.36951	0.1782488
2.5	1.82885	0.0428452	102.9565	0.2248665
2.75	2.882083	0.0627435	110.1975	0.2769205
3	4.270422	0.0882087	117.1257	0.3343412
3.25	6.021963	0.1199027	123.7696	0.3970489
3.5	8.155166	0.1584495	130.1537	0.4649562
3.75	10.67935	0.2044314	136.2996	0.5379711
4	13.59569	0.2583873	142.2259	0.6159979
4.25	16.89824	0.3208123	147.9492	0.6989388
4.5	20.57526	0.3921575	153.484	0.7866935
4.75	24.61028	0.472832	158.8435	0.8791628
5	28.98331	0.5632037	164.0393	0.976247
5.25	33.67171	0.6636012	169.0818	1.077846
5.5	38.65118	0.7743158	173.9804	1.183862
5.75	43.89635	0.8956046	178.7435	1.294107

Buttons: Scala CSA, Conc vs. Time, Conc vs. Distance, Script Commands, 3D Data, Save, Perfusion Arrays (Parrav, Injection, Sampling, Peri Flow, Peri Leak)

The Text Page allows a variety of data to be viewed and/or saved as a .csv file and viewed in Excel or any text editor via the “Save” button.

The “perfusion arrays” option is for debugging the program and is not discussed here.

### Using the Command Line Interface (CLI)

The Command window is at the left of the screen and serves several purposes.

1. **Notification** - It is programmed to notify the user when an important event has taken place during a simulation or action by the user is completed. When a notification occurs a message on the CLI is posted. During a scripted simulation the CLI may output messages similar to this -

```
>>EVENT - **Simulating**
>>EVENT - RWgo is ON at 0min (0sec)
>>EVENT - Stapesgo is ON at 0min (0sec)
>>EVENT - RWgo is OFF at 30min (1800sec)
>>EVENT - Stapesgo is OFF at 30min (1800sec)
>>EVENT - Simulation Complete
```

The “EVENT” message notifies the user that an important event has taken place during the simulation at a given time. In this example the Round Window and Stapes applications are ON at the start of the simulation and OFF after 30 minutes.

2. **Commands** - Actions can be initiated through a list of commands.

The CLI prompt is a two caret symbol “>>”. All commands should be entered to the right of the LAST >> symbol in the box.

Commands are single word texts which give the user the ability to load/save parameters, initiate a simulation, print out current parameter values, and more. Here is a list of commands, which can also be found by typing in the the word “help” in the command box. Remember, the CLI is NOT case sensitive, so as long as the spelling and format are correct the command will be initiated, otherwise, an error message will occur.

SaveParams - Saves all current parameters to a text .csv file  
LoadParams - Loads a parameters .csv file and parses all containing variables, clearing all current variables  
Print - Prints a list of the values for each possible variable  
SaveScript - Saves a current script that was written in a text .csv file  
ClearScript - Clears a current script (the simulation will ALWAYS read from the most current script so this command must be done if you want to run an unscripted simulation)  
LoadScript - Loads a .csv script file and clears the current one  
Simulate - Runs a simulation with all current variables set  
ViewText - Opens text window to see CSAs, concentrations, measurement DATA, scripts, and 3D data

3. **Setting Variables** - Most parameters can be set through the CLI. Unlike commands which only contain a single word, a variable contains two parts: the variable name and the value. These parts are separated by a comma and must both have correct format and spelling for the variable to be set. For example, to set the variable “TimeVal” (which is the total time to calculate) to 100 minutes the user would write “TimeVal, 100” and a value of 100 minutes would be input into the time to calculate box in the main control bar. This works for every user editable parameter in the program. For turning on or off checkboxes the integer value of 1 or 0 is used respectively. To turn on the round window application via the CLI one would write “RWgo, 1” and to turn it off “Rwgo, 0”. Below is a list of the available variables that can be set.

\*\*\*General\*\*\*

TimeVal - The total simulation time  
DVal - Diffusion Coefficient  
PauseTime - time to pause during a simulation

\*\*\*Iontophoresis\*\*\*

IontoGo - Turns Iontophoresis on/off via values '1' or '0'  
IontoLoc - Iontophoresis injection location (mm)  
IontoI - Iontophoresis current (nA)  
IontoTN - Iontophoresis transport number  
Ionto12 - Iontophoresis half time (min)  
IontoScala - Iontophoresis injection scala

\*\*\*Injection\*\*\*

InjGo - Turns Injection on/off via values '1' or '0'  
EntryScala - Injection entry scala  
ExitScala - Injection exit scala  
EntryLoc - Entry location (mm) of entry scala  
ExitLoc - Exit location (mm) of exit scala  
InjConc - Injection concentration  
InjRate - Injection uLiters per minute  
InjExp - Exponential On/Off t1/2 (min)

\*\*\*Round Window\*\*\*

RWGo - Turns round window application on/off via values '1' or '0'  
InitConc - Initial middle ear concentration  
RWarea - Area of round window (mm<sup>2</sup>)  
RWdist - Distance projected  
RWperm - Round window permeability  
RWvol - Volume applied to middle ear (uLiters)  
RWvolClear - Volume clearance half time (min)  
RWdrugClear - Druge clearance half time (min)

\*\*\*Stapes\*\*\*

StapesGo - Turns stapes application on/off via values '1' or '0'  
StapesPerm = Stapes permeability  
StapesArea - Area of stapes footplate(mm2)  
StapesDist - Distance projected

\*\*\*Sampling\*\*\*

PSampleOn - Turns perilymph sampling on/off via values '1' or '0'  
PSampScala - Scala being sampled  
PSampLoc - Location (mm) on scala being sampled  
SampTime - Time at which sampling takes place (if more than one time in form of 30, 90, 120, etc.)  
Sampling - The sampling variable takes two values in the form 'Sampling, 30, 1'. The first is the duration of each sample (min) and the second is the volume(uL)  
SampNum - Number of samples taken at each sample time

\*\*\*Perilymph Flow\*\*\*

FlowOn - Turns perilymph flow on/off via values '1' or '0'  
FlowRate - Rate of perilymph flow (uLiters per min)

\*\*\*Perilymph Leak\*\*\*

LeakOn - Turns perilymph leak on/off via values '1' or '0'  
LeakScala - Scala where leak occurs  
LeakLoc - Location (mm) on scala where leak occurs  
LeakRate - Rate (uLiters per min) at which leak occurs, a negative rate calculates solute leaking into the scala at a concentration equal to the concentration of blood.

\*\*\*Cochlear Implant\*\*\*

CIOn - Turns CI injection method on/off via values '1' or '0'  
CIStartPt - The location on ST where the CI is being inserted  
CIEndPt - The location on ST where the CI will stop being inserted once it's tip has reached it  
CImoveRate - The rate in mm/sec at which the CI is inserted  
CIconc - The concentration of solute inside the CI  
CIFlowOut - Turns flow out of the cochleostomy on/off via values '1' or '0'  
CIPercentOut - Percentage of solute flowing out of the cochleostomy  
CIFlowIn - Turns flow to the apex on/off via values '1' or '0'  
CIDrag - Turns ability of CI to drag solute on/off via values '1' or '0'  
CIDragArea - The amount of area included in the drag  
CIRate - The rate at which the solute diffuses out of the CI

4. **Writing Scripts** - In FluidSim3.0 it is possible for the program to change values to any of the above parameters automatically during a simulation through scripts. Scripts are very similar to setting variables, except a third condition is included: the time at which the variable should be set. This time is written before the variable name and its value and again separated by a comma. For example, to turn the Round window application on at the start of the simulation and off after 30 minutes the script would look like this

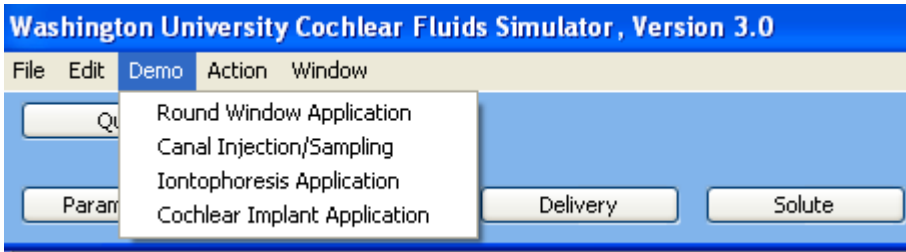
```
>>>0, RWgo, 1  
>> 30, Rwgo, 0
```

At 0 minutes round window is ON  
At 30 minutes round window is OFF

When a variable is scripted it is saved as a time command. All of the time commands saved by the program can be viewed by going to the “View Text” window and clicking on “Time Commands” at the bottom left hand corner. You can also remove individual statements of script here by clicking on a line and pressing delete or backspace. The script's statements do not need to be in sequential order. In other words it does not matter where the statement lies in the script as long as it is labeled with the appropriate time. The CLI command “ClearScript” clears all of the time commands. If you quit the application via the “Quit” button on

the main control bar or save parameters via the command “SaveParams” all of the current time commands are saved. Scripting is very useful when running a complicated simulation multiple times, otherwise everything can be done manually by pressing Pause or setting a pause time and altering the variables via the GUI before resuming.

## Demonstrations



From the upper menu bar a number of “demonstrations” can be selected. Each demonstration loads a parameter file, which may include script commands.

These demonstrations are intended to show the capabilities of the program and the parameters are not intended as appropriate for the specific protocol. The parameter files can be modified as the user wishes.

## Bugs and Issues

The parts of the program that we have been actively using have been well tested and are relatively bug-free. However, there are many configuration, representing “unusual protocols” that have not been tested. If the program gives errors for you in setting up a certain configuration, please let me know and I’ll try and fix it. If you can send me the parameter file (saved with saveparams in the command window), it may help replicate the problem.

One occasional problem (usually in Windows) is that the program sometimes wants to load a file and comes up in the wrong directory. In most cases, this is solved by selecting the Fluidsim3 directory.

## Files

Parameters and configurations are stored as \*.csv (comma separated text) files. You can view and edit these files in Excel (or similar) but make sure they are saved back as .csv format. The program saves the current configuration, so it starts up as you left it.

“Startup\*\*\*” files contain the setup for each “Animal” configuration

Startup.csv contains a single line, which is the default Animal configuration

“CI\*\*\*\*.csv” files contain cochlear implant configurations.

“Demo\*\*\*\*.csv” are the Demo setup files

“Easy\*\*\*\*.csv” files are the easy setup parameters for some substances

Guinea Pig\*\*\*, Human\*\*\* and Tubes files are area and interaction files. These should not be changed unless you know what you are doing :)

Fixedparams.csv contains diffusion coefficients and other data. It can be edited (to add new diffusion coefficients), but if you corrupt it, the program may not run.

