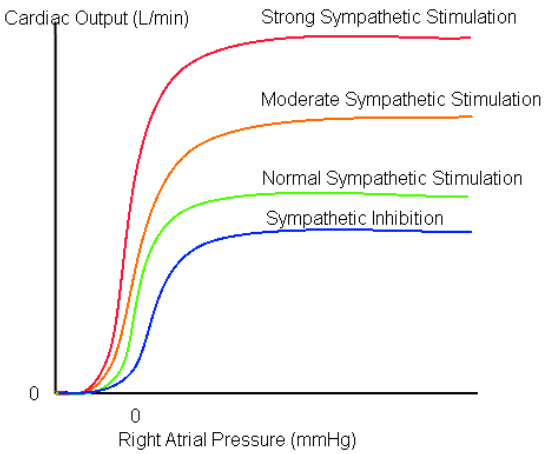
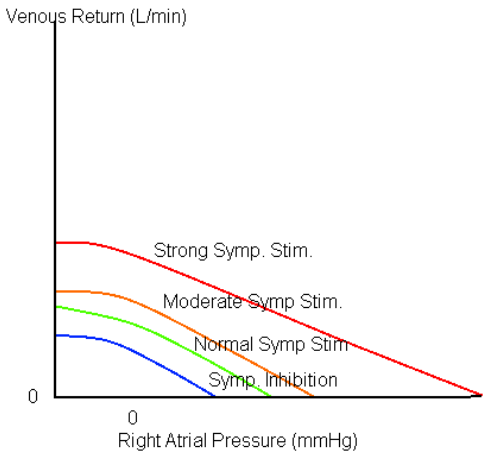
Conceptually Diagnosing Cardiac Malfunction

Cardiac Output and Venous Return Curves for Various Stimulations

Since Cardiac Output = HR* SV, sympathetic stimulation will increase cardiac output as it increases both heart rate and stroke volume. The greater the stimulation, the greater the cardiac output. Inhibition of sympathetic stimulation will result in a decrease in cardiac output.





Sympathetic stimulation decreases venous compliance, increasing central venous pressure, resulting in increased venous return at any given right atrial pressure value. This is because the pressure gradient (difference between veins and atrium) is increasing and forces the entry of more blood before the pressure gradient is equalized, as well as the increased venous pressure expands the veins and decreases resistance permitting higher flow rates.

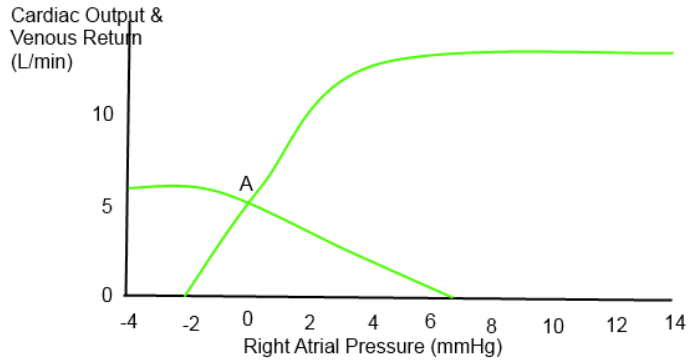
Moderate Heart Failure (from onset to compensation):

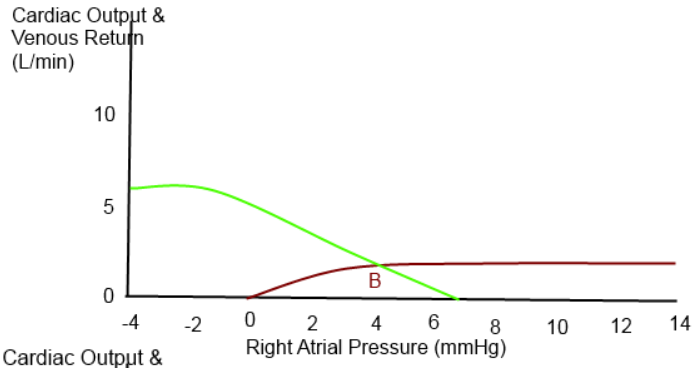
The heart starts at a healthy cardiac output and venous return shown below at point A

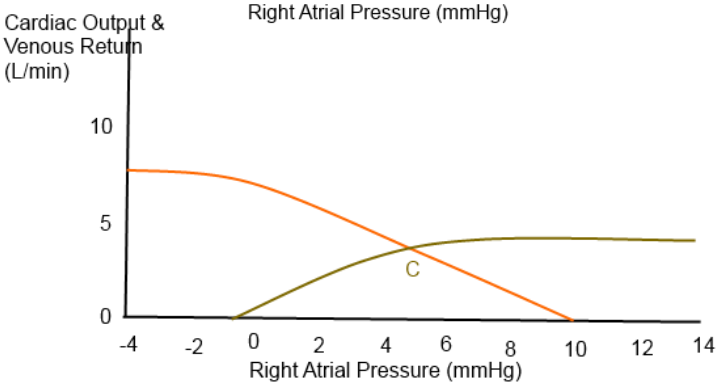
Then moderate heart failure onsets… and immediately proper heart pumping function is drastically reduced shifting the entire cardiac output curve down. This makes the intersection of the cardiac output and venous return (where homeostasis exists) shift down and to the right to point B since the venous return hasn't changed yet.

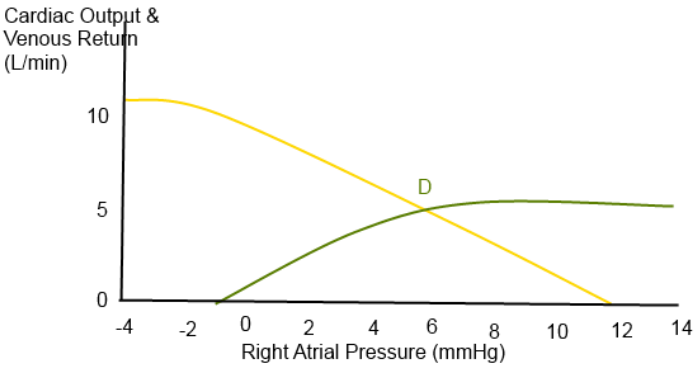
When cardiac output drops, the venous pressure begins to increase due to damming of blood in the veins. By the logic of problem 1 this will increase venous return and the entire curve shifts up. The body responds to baroceptors and reduced blood flow to the CNS by increasing sympathetic stimulation and inhibiting vagal stimulation. This increases the cardiac output by the logic of problem 1. These two functions combined (increased venous return by increased systemic filling pressure and compensatory increase in cardiac output) cause a new temporary equilibrium at point C.

Chronic recovery begins, leading to compensation for the heart failure. This includes renal retention of fluids, increase in blood volume and the gradual with-drawl of the autonomic responses all occurring over larger time scales (with very long timescales for the autonomic with-drawl). Equilibrium shifts from C to D.





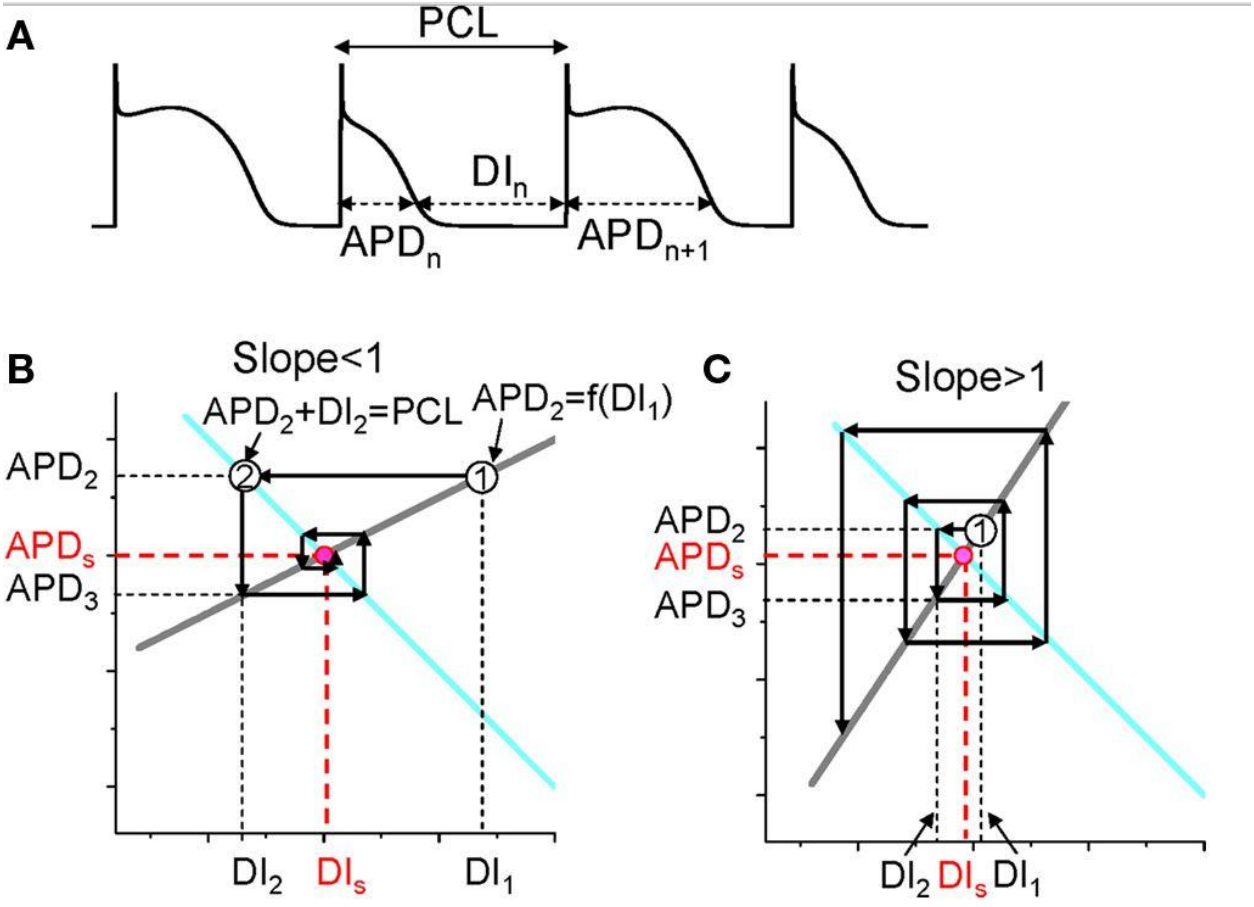




Dominant Pacemaker Concept:

A properly functioning heart is controlled by one pacemaker in a hierarchy of automaticity foci. The dominant pacemaker is always the function automaticity foci with the most rapid intrinsic rate. In a properly functioning heart the dominant pacemaker should reside in the SA node which can receive modulatory effects from sympathetic and parasympathetic stimulation pathways. The hierarchy below the SA node jumps to other atrial automaticity foci, then a junctional automaticity foci, and finally a ventricular automaticity foci. Without the presence of any blocks, the pacing of all automaticity foci lower on the hierarchy than the currently active pacemaker are "over-drive suppressed" by the active dominant pacemaker.

Restitution Hypothesis of Block of Conduction and Onset of Reentry:



It is easiest to explain the restitution hypothesis with the help of a simplified (linear) restitution curve. Most simply, the convergence of the left plot implies stability. The APD has an oscillation of decreasing amplitude until it reaches a steady state value. The right plot diverges, implying instability, oscillation grows if APD grows. Reentry implies there is a blocking of conduction (slow-down of conduction) because the APD keeps increasing. As the APD increases, the DI decreases leading to less effective heart

pumping action. This increase in APD continues until you get a wave break which can complete the block of conduction and can cause fibrillation.

Notes and further reading on the Restitution Hypohtesis:

http://journal.frontiersin.org/Journal/10.3389/fphys.2010.00154/full

Restitution describes the dependence on both the cardiac AP duration and the diastolic interval. The relationship between the AP duration and the diastolic duration can lead to arrhythmias. If you end up with an unstable wave (when you have a wave break, with uneven depolarization) the general trend is that as the diastolic interval decreases, so does the AP duration. You can plot a restitution by plotting AP duration as a function of the diastolic interval. Looking at that curve, looking at the slope as less than and greater than 1, it will create either unstable or stable depolarization.

http://www.ncbi.nlm.nih.gov/pubmed/9887041

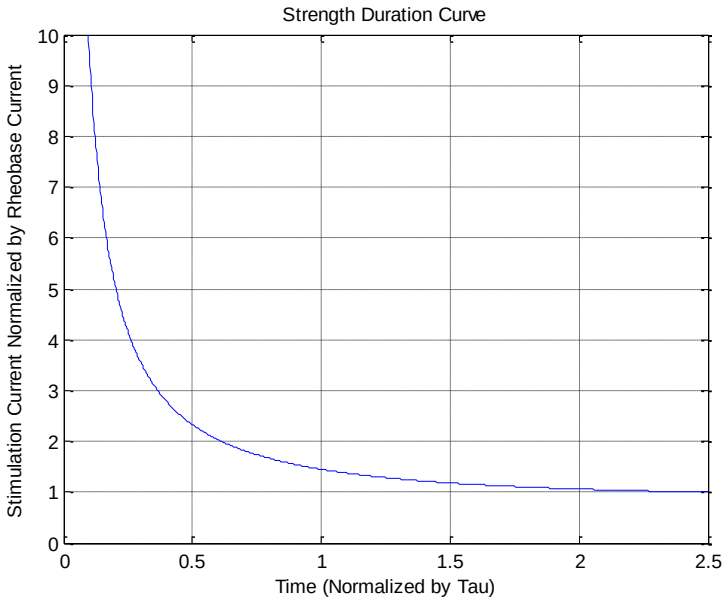
starting at a point on the restitution curve, how does the system respond

http://www.scholarpedia.org/article/Cardiac_arrhythmia#Functional_reentry:_spiral_and_scroll_waves

http://www.math.utah.edu/~keener/classes/math5110/extra_class_notes/apd_map.pdf

http://journal.frontiersin.org/Journal/10.3389/fphys.2010.00154/full (see figure 2)

Plotting the strength duration curve of a spherical excitable cardiac cell:



http://www.ece.mcmaster.ca/faculty/debruin/EE%20795/ECE795_lecture2.pdf

Rheobase is a way of measuring how excitable a membrane is. It is defined as the minimal amplitude of an indefinite duration applied current that results in the raising of membrane potential to depolarization threshold (ie: initiating an action potential).

Chronaxie: time required for current to reach 2*rheobase (to effectively stimulate a cell)

```
close all; clear all; clc;

%From Source
% The mean membrane time constant was 70 msec. and the input resistance was
% about 8 Mohm. The specific membrane resistance (Rm) and capacity (Cm)
% were 20 000 ohm.cm2 and 5--6 muF/cm2, respectively. After glycerol
% treatment the Rm decreased to 10 000 ohm.cm2 and the Cm to 4--4.5 muF/cm2.

delta_V_th = 0.005;  %mV
cell_SA = 0.0000035; %surface area of myocte (cm^2)
% radius = 50*10^-4; % (cm) radius of a spherical representation of the cell
% cell_SA = 4*pi*radius^2;

specific_R_m = 20000; %specific membrane resistance (Ohms*cm^2)
R_m =  specific_R_m / cell_SA; % Membrane resistance (Ohms)

specific_C_m =  5.5*10^-6; %Specific Membrane capacitance  F/cm^2
C_m = specific_C_m*cell_SA;%Membrane capacitance (F)

% tau = specific_R_m*specific_C_m;
tau = R_m*C_m;
t = linspace(0,2.5*tau,1000);

for i=1:length(t)
%     I_s(i) = delta_V_th/(specific_R_m*(1-exp(-t(i)/tau)));
    I_s(i) = delta_V_th/(R_m*(1-exp(-t(i)/tau)));
end

figure;
```

```
plot(t/tau, I_s/I_s(length(I_s)));
grid on;
axis([0,2.5,0,10]);
title('Strength Duration Curve');
xlabel('Time (Normalized by Tau)');
ylabel('Stimulation Current Normalized by Rheobase Current');
```