BIO 5329: PROBLEM SET 3

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Due at the start of class on November 1. Please hand in the analytical problems in class and e-mail the *well-commented* Matlab M-files to me (baker@ccb.wustl.edu) before class.

1. Orthogonal bases (20 points)

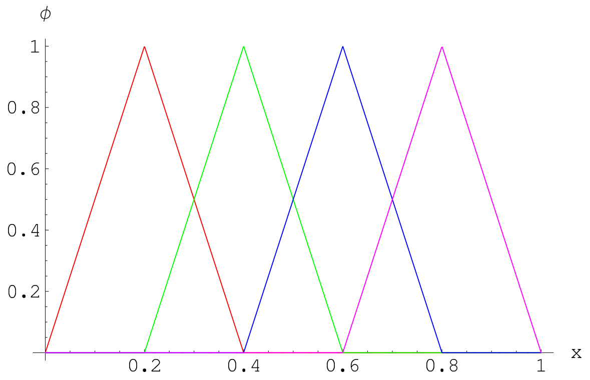
Finite elements are a popular and powerful way to solve a number of problems in the biological sciences and engineering. The simplest finite element basis set consists of piecewise linear elements on uniformly-spaced intervals. The reference basis function has the form:

$$\phi(y;h) = \begin{cases} \frac{y+h}{h} & -h \le y \le 0 \\ \frac{h-y}{h} & 0 \le y \le h \end{cases} \tag{1.1}$$

Individual basis functions are formed by translation of this reference basis function:

$$\phi_n(x;h) = \phi(x - nh; h); \tag{1.2}$$

e.g., ϕ_0 is non-zero over $[-h, h]$, ϕ_1 is non-zero over $[0, 2h]$, ϕ_n is non-zero over $[(n-1)h, (n+1)h]$. Suppose we want to use 4 of these basis functions with $h = 1/5$ to represent functions $f(x)$ on the interval $[0, 1]$ which have the properties $f(0) = 0$ and $f(1) = 0$. This set of basis functions looks like:



However, this set of basis functions is not orthogonal! Your job is to:

(a) (8 points) Generate a new orthonormal set of basis functions and draw a picture to indicate what new set looks like. You can either do this by hand or by implementing the Gram-Schmidt algorithm in Matlab. Be sure to include code or calculations that demonstrate the orthnormality of the resulting basis functions. **NOTE**: If you use Matlab, you *may not* use the `orth` function.

(b) (4 points) Represent $f(x) = 4x - 4x^2$ in this your orthonormal basis as the approximate function

$$\tilde{f}(x) = \sum_{i=1}^{4} \alpha_i w_i(x), \tag{1.3}$$

where w_i are the orthonormal basis functions. **HINT**. It may help to plot the original function and your approximation to check your answer. **NOTE**. If you couldn't find the orthonormal basis functions in the previous step, try to represent the above function in the original finite element basis. If you are really ambitious, you can calculate the error in this approximation $\left\| f - \tilde{f} \right\|_{L^p}$, for $p = 1$, 2, or ∞.

(c) (8 points) The "mass matrix" $\underline{\underline{M}}$ has elements

$$M_{ij} = \int_\Omega \phi_i(x)\phi_j(x)dx \tag{1.4}$$

which describe the overlap between two basis functions ϕ_i and ϕ_j over the domain Ω ($\Omega = [0,1]$ in the current problem). We've already established that our finite element basis above is not orthonormal. Suppose we want to find a new basis

$$\psi_n(x) = \sum_i^N \alpha_{in}\phi_i(x) \tag{1.5}$$

which is orthonormal; e.g.,

$$\int_\Omega \psi_n(x)\psi_m(x)dx = \delta_{nm} \tag{1.6}$$

where δ_{nm} is the Kronecker delta symbol. Let $\underline{\underline{A}}$ be the matrix with elements $A_{ij} = \alpha_{in}$. Let $\underline{\underline{B}} = \underline{\underline{A}}^{-1}$. Prove that

$$\underline{\underline{B}}^\dagger \underline{\underline{B}} = \underline{\underline{M}} \tag{1.7}$$

where $\underline{\underline{B}}^\dagger$ is the transpose of $\underline{\underline{B}}$.

This factorization

$$\underline{\underline{B}}^\dagger \underline{\underline{B}} = \underline{\underline{M}} \tag{1.8}$$

is called the Cholesky decomposition of $\underline{\underline{M}}$ and offers an alternative to Gram-Schmidt for larger bases. There are many numerical methods to perform the Cholesky decomposition in a much more stable manner than Gram-Schmidt. Use Matlab's `chol` implementation of the Cholesky decomposition to orthogonalize the finite element basis. Compare your answer to the results of the Gram-Schmidt method.

2. POISSON'S EQUATION (20 POINTS)

(a) (5 points) Many problems in linear algebra are inspired by energy minimization. In particular, we usually begin with an energy functional of the form

$$G[\,\underline{u}\,] = \frac{1}{2}\,\underline{u}^{\dagger}\,\underline{\underline{A}}\;\underline{u} - \underline{b}^{\dagger}\,\underline{u}\,, \tag{2.1}$$

and asked to find $\underline{x}$ which minimizes (or at least extremizes) this energy functional. Show that extremization of this energy function leads to the linear equations

$$\underline{\underline{A}}\;\underline{v} = \underline{b} \tag{2.2}$$

where $\underline{v}$ is the location of the extremum of G. Assume $\underline{\underline{A}}$ is symmetric.

(b) (5 points) Now we'll consider specific forms of $\underline{\underline{A}}$ and $\underline{b}$. Consider the domain $\Omega = [0,1]$ and a basis set $\{\sqrt{2}\sin(n\pi x)\}$ for $n = 1, 2, 3, \ldots, N$. Let $\underline{\underline{A}}$ be the matrix resulting from the projection of the operator

$$\mathcal{A} = -\nabla^2 \tag{2.3}$$

on this basis and let $\underline{b}$ be the vector resulting from the projection of the function

$$f(x) = \frac{1}{2}x - \frac{3}{2}x^2 + x^3 \tag{2.4}$$

on this basis. Write expressions for A_{ij} and b_i.

(c) (5 points) Use your definitions of $\underline{\underline{A}}$ and $\underline{b}$ from above to solve

$$\underline{\underline{A}}\;\underline{v} = \underline{b} \tag{2.5}$$

for $\underline{v}$. Represent the solution to

$$-\nabla^2 v(x) = f(x) \tag{2.6}$$

using the sine basis above with $N = 20$ basis functions. Compare the solution in this sine basis to the analytical solution

$$v(x) = -\frac{1}{120}\left(-x + 10x^3 - 15x^4 + 6x^5\right). \tag{2.7}$$

3. OVERDAMPED DYNAMICS (20 POINTS)

A deterministic system with N degrees of freedom in a highly-viscous medium evolves in time as

$$\dot{\underline{x}}\,(t) = \underline{\underline{D}}\ \underline{f}\,(t) \tag{3.1}$$

where, $\underline{x}\,(t)$ is a length-N vector of positions, $\underline{\underline{D}}$ is a time-independent $N \times N$ symmetric diffusion coefficient matrix and $\underline{f}\,(t)$ is a length-N time-dependent force vector.

(a) (5 points) Suppose that $\underline{x}\,(t)$ represents the deviation of a set of particles with positions $y_i(t)$ from their equilibrium positions $\overline{y}_i$ such that

$$x_i(t) = y_i(t) - \overline{y}_i. \tag{3.2}$$

Assume that the energy $H(\,\underline{x}\,)$ associated with the deviation from equilibrium is harmonic (e.g., we have a set of springs)

$$H(\,\underline{x}\,; t) = \frac{1}{2}\sum_i \sum_j k_{ij} x_i(t) x_j(t) \tag{3.3}$$

where $k_{ij} = k_{ji}$ are the elements of a symmetric "stiffness" matrix $\underline{\underline{K}}$. Using the fact that

$$f_i = -\frac{\partial H}{\partial y_i}, \tag{3.4}$$

write an expression for $\underline{f}\,(t)$ as a function of $\underline{\underline{K}}$ and $\underline{x}\,(t)$.

(b) (5 points) Using your answer for the previous step, the equation of motion (Eq. 3.1) should have the form

$$\dot{\underline{x}}(t) = \underline{\underline{A}}\,\underline{x}(t) \tag{3.5}$$

where $\underline{\underline{A}}$ is determined by your expression for $\underline{f}$ left-multiplied by $\underline{\underline{D}}$. This looks like a hard differential equation since $\underline{\underline{A}}$ is a dense matrix and induces lots of coupling between the elements of $\underline{x}$. Convert this equation to a simpler problem of the form

$$\dot{\underline{z}}(t) = \underline{\underline{B}}\,\underline{z}(t) \tag{3.6}$$

where $\underline{\underline{B}}$ is a diagonal matrix and $\underline{z}(t) = \underline{\underline{C}}\,\underline{x}(t)$, where $\underline{\underline{C}}$ a matrix (that you need to find).

(c) (5 points) Solve

$$\dot{\underline{z}}(t) = \underline{\underline{B}}\,\underline{z}(t) \tag{3.7}$$

for $\underline{z}(t)$ using the $\underline{\underline{B}}$ and $\underline{z}(t)$ you found in the previous step. Use the initial condition

$$\underline{z}(0) = \underline{z}_0. \tag{3.8}$$

(d) (5 points) Implement your solution for $\underline{x}(t)$ in Matlab for $N = 10$ for a homogeneous diffusion coefficient $D_{ij} = \delta_{ij}$, where δ_{ij} is the Kronecker delta symbol, a chain of springs where each spring is coupled to its nearest neighbor

$$K_{ij} = \begin{cases} 1 & i = j \\ \frac{1}{2} & j = i+1, i < N \\ \frac{1}{2} & j = i-1, i > 1 \\ 0 & \text{otherwise,} \end{cases} \tag{3.9}$$

and a inital displacement of

$$(x(0))_i = \begin{cases} 1 & i = 1 \\ 1 & i = N \\ 0 & \text{otherwise.} \end{cases} \tag{3.10}$$

4. NULL SPACES IN (BIO)CHEMICAL KINETICS (20 POINTS)

The null space of an operator is a rather abstract concept. As we discussed in class, this space has a non-zero dimension (nullity) when the operator cannot be inverted; e.g., when more than one solution might exist. Here, we'll discuss two physically-relevant nullspaces related to chemical kinetics:

(a) (10 points) Consider the system of unimolecular reactions

$$M_1 \overset{k_{12}}{\rightarrow} M_2 \tag{4.1}$$

$$M_2 \overset{k_{21}}{\rightarrow} M_1 \tag{4.2}$$

$$M_3 \overset{k_{31}}{\rightarrow} M_1 \tag{4.3}$$

$$M_3 \overset{k_{32}}{\rightarrow} M_2 \tag{4.4}$$

$$M_4 \overset{k_{41}}{\rightarrow} 2M_1 \tag{4.5}$$

where M_i indicates different states of a molecule. If we know all the rates, we can write a series of ordinary differential equations governing the fraction $c_i(t)$ of state i at time t as:

$$\dot{c}_1(t) = -k_{12}c_1(t) + k_{21}c_2(t) + k_{31}c_3(t) + 2k_{41}c_4(t) \tag{4.6}$$

$$\dot{c}_2(t) = k_{12}c_1(t) - k_{21}c_2(t) + k_{32}c_3(t) \tag{4.7}$$

$$\dot{c}_3(t) = -k_{31}c_3(t) - k_{32}c_3(t) \tag{4.8}$$

$$\dot{c}_4(t) = -k_{41}c_4(t) \tag{4.9}$$

which can be rewritten as

$$\dot{\underline{c}}\,(t) = \underline{\underline{K}}\ \underline{c}\,(t). \tag{4.10}$$

Find a steady-state solution for this system $\dot{\underline{c}} = 0$ in the null space of $\underline{\underline{K}}$.

(b) (10 points) When the rate constants aren't known, it's still possible to get an idea of the steady state behavior of the system through a technique that's often called "metabolic flux analysis". Consider the same reactions as above, now given indices:

$$M_1 \rightarrow M_2 \text{ (Rxn 1)} \tag{4.11}$$

$$M_2 \rightarrow M_1 \text{ (Rxn 2)} \tag{4.12}$$

$$M_3 \rightarrow M_1 \text{ (Rxn 3)} \tag{4.13}$$

$$M_3 \rightarrow M_2 \text{ (Rxn 4)} \tag{4.14}$$

$$M_4 \rightarrow 2M_1 \text{ (Rxn 5).} \tag{4.15}$$

Each reaction i can be assigned a velocity r_i such that the flux of species j due to reaction i has the form

$$J_{ji}(t) = n_{ji} r_i(t) \tag{4.16}$$

where n_{ji} is the stoichiometry of species j in reaction i. The rate of change in the concentration of species of j is then given by

$$\dot{c}_j(t) = \sum_i J_{ji}(t) = \sum_i n_{ji} r_i(t). \tag{4.17}$$

For the current system, we have

$$\begin{aligned} \dot{c}_1(t) &= -r_1(t) + r_2(t) + r_3(t) + 2r_5(t) && (4.18) \\ \dot{c}_2(t) &= r_1(t) - r_2(t) + r_4(t) && (4.19) \\ \dot{c}_3(t) &= -r_3(t) - r_4(t) && (4.20) \\ \dot{c}_4(t) &= -r_5(t). && (4.21) \end{aligned}$$

As usual, we want to examine the system at steady-state

$$\dot{c}_j(t) = 0, \tag{4.22}$$

but, for this method, in terms of the reaction rates r_i instead of the concentrations. Represent this method as a nullspace problem of the form

$$\underline{\underline{N}}\, \underline{r} = 0 \tag{4.23}$$

and show that the results are consistent with the answers from the previous question.

5. Inverses (20 points)

Suppose you have gone to great effort to solve a linear algebra problem

$$\underline{\underline{A}}\,\underline{x} = \underline{b} \tag{5.1}$$

for a symmetric matrix $\underline{\underline{A}}$ and thereby obtained

$$\underline{x} = \underline{\underline{A}}^{-1}\underline{b}. \tag{5.2}$$

Now you want to solve a very similar problem (perhaps a fitting problem where a few additional data points have been obtained)

$$\left(\underline{\underline{A}} + \epsilon\,\underline{\underline{B}}\right)\underline{y} = \underline{b} \tag{5.3}$$

where ϵ is very small. Perform a Taylor series expansion of $\left(\underline{\underline{A}} + \epsilon\,\underline{\underline{B}}\right)^{-1}$ by expanding with respect to ϵ around 0. Write your answer in terms of $\underline{b}$, $\underline{\underline{A}}$, $\underline{\underline{A}}^{-1}$, and $\underline{\underline{B}}$ and include terms up to the order of ϵ. **HINTS:**

- Matrices can be differentiated in an element-wise fashion.
- Derivatives of a matrix inverse is most easily derived from the relationship $\underline{\underline{A}}\,\underline{\underline{A}}^{-1} = \underline{\underline{I}}$.