California State University, San Bernardino
Computer Science Department

Thesis Preliminary Proposal

For

pCT

By

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1. INTRODUCTION

1.1 Background

Proton computed tomography (pCT) has been explored in the past decades because of its unique imaging characteristics, low radiation dose, and its possible use for treatment planning and on-line target localization in proton therapy [24], [8]. The use of protons for medical imaging was suggested many years ago [15, 13] but pCT was never fully developed because of great advances in x-ray CT (xCT) and other imaging modalities. In recent years, pCT has gained relevance because proton treatment centers opened and rotatable proton gantries became available [23, 24].

Proton therapy is an advanced form of adiation therapy which offers proven advantages in radiation therapy (Hug 2004). Currently x-ray CT is used for proton treatment planning, which has disadvantages, e.g., the mapping from Hounsfield values to electron density is not unique (Saw 2005). In addition, x-ray CT is now used in the treatment room to image the patient in the treatment position relative to the radiation beam; however, this requires careful alignment between the x-ray source and the treatment radiation source.

pCT in these applications would be advantageous because it directly reconstructs the electron density values and uses the same radiation source that is being used for treatment. Therefore, pCT in combination with proton radiation therapy may lead to ultimate form of image-guided radiotherapy. pCT is based on the same underlying principles as other medical imaging modalities but differs in some other aspects. pCT measures the energy loss rather than the attenuation of protons. From this information, the integrated density along the proton path can be estimated. The most important difference with respect to xCT is that protons undergo multiple scattering inside the object and, therefore, follow paths that statistically deviate from straight lines.

The pCT reconstruction problem also differs in some respects from that of xCT, PET, and SPECT. In xCT, data collection is usually considered as the Radon transform, i.e., the integration along straight lines of the object source function. In this case, the object data represent the attenuation coefficient map and the projection data the log values of the detected x-ray counts. In pCT, protons with known entry energy are tracked individually on the entry and exit side of the object and their outgoing energy is recorded. This can be achieved with modern particle tracking detectors developed for high-energy physics applications. Because of the random nature of proton scattering, it is not possible to calculate the precise trajectory of the protons within the target, but the entry and exit locations and directions of the protons can be used to estimate their path through the object, and the measured energy loss permits estimating the integrated electron density along the proton path.

The main goal of pCT for therapy applications is to determine of the object electron density. The image reconstruction problem for pCT is then to obtain the best estimate for the relative electron density map from the measured proton data. The problem is not exactly solvable because of two factors: (1) the statistical fluctuation of the measured energy loss mainly due to energy straggling, and (2) the statistical deviation of the proton from its most likely path (MLP) due to multiple Coulomb scattering.

A major problem that needs to be solved is finding an optimized reconstruction algorithm. Researchers, using GEANT4 and an elliptical object model have shown that, in principle an algebraic reconstruction technique (ART) leads to a good spatial resolution (T. Li 2006) [27]. However, there are many different algebraic reconstruction techniques (also called series expansion methods) which have not been explored. These may differ in terms of computer speed, possibility to perform parallel computations, and the accuracy of the reconstruction. This will be explored in this thesis work.

1.2 Significance

1.3 Purpose

Although a considerable amount of research has been done already in this field, much is left to be researched and novel techniques to be developed and new findings to be discovered. Previous work clearly points to series expansion methods, but so far only one technique (additive ART) has been tried. Other series expansion techniques may give better results. These techniques have parameters that can be optimized, which has not been done yet.

Furthermore, reconstruction has been done only in a 2-D object, this needs to be extended to a 3D objects. One of the challenges of the series expansion techniques is their high computation cost (e.g., twelve hours computation time for a MLP reconstruction on a laptop PC (Li 2006)). This could be accelerated using parallel computing techniques and/or hardware accelerators. Another problem is the fact that the performance of these algorithms will depend on the choice of relaxation factors and the particular image type. Therefore, more research is clearly needed to study the accuracy of these techniques and to optimize their performance.

The results of this work will have important implications in proton therapy planning and image-guided proton therapy.

1.4 Research Execution Plan

In this research I will researching various series expansion reconstruction techniques for pCT. In particular, I will perform the following tasks: " The first step involves implementation of various pCT reconstruction algorithms in 2-D and testing their performance with GEANT4-simulated pCT data. I will optimize the performance by systematically varying relaxation parameters and iterative refinement steps. This first task is anticipated to take about 4 months. " The second step is to improve the timing of the selected 2-D algorithm using numerical and parallel processing techniques. This is anticipated to take about 4 months. " The third step is to extend the optimized 2-D algorithm to three-dimensional objects. This is anticipated to take two months. " After conclusion of these steps, I will suggest the path to be followed from that point on. I will look at possible hardware implementation using Field Programmable Gate Array (FPGA), Digital Signal Processing (DSP), and Graphics Processing Unit (GPU) to speed up the process. Some basic tests and analysis will be performed for one month. During the final month, conclusions will then be drawn and recommendations for further work be given.

2. TEST OF VARIOUS NUMERICAL INTEGRATION ALGORITHMS TO CONVERT PROTON ENERGY LOSS TO INTEGRATED DENSITY

2.1 Introduction and background

The main principle of proton CT is based on the determination of the integrated volume electron density, ρ_e (or short, the electron density) by measuring the energy loss of protons after traversing the image object. The electron density of a material is defined as the number of electrons/cm^3.

The relationship between volume electron density and physical density is given by

$$\rho_e = \rho N_A \left(\frac{Z}{A}\right) \tag{2.1}$$

where ρ is the physical density, N_A is Avogadro's number (6.023×10^{-23}), Z and A are the (effective) atomic number and atomic weight of the traversed material, respectively. When the object material is comprised of a compound, for example, water (H_2O), or a mixture of elements or compounds, the electron density is given by:

$$\rho_e = \rho N_A \Sigma_i w_i \frac{Z_i}{A_i} \tag{2.2}$$

where w_i is the fraction by weight of element i, and Z_i and A_i are the atomic number and atomic weight of the ith element. The elemental and compound data required for these calculations may be obtained from NIST [14, 22].

Since the ratio Z/A is fairly constant for human tissues, the electron density closely reflects the physical density of the imaged tissue[26]. To avoid the large numbers associated with absolute volume electron density values (which are of the order of 1023 electrons/cm3) it is better to express results in terms of relative volume electron density, which is defined as:

$$\eta_e = \frac{\rho_e}{\rho_{e,water}} \tag{2.3}$$

where $\rho_{e,water} = 3.343 \times 10^{23} electron/cm^3$ is the volume electron density of water.

The energy loss per unit track length of a proton, also called the stoping power ıS, is described by the Bethe Bloch equation [20] as

$$\begin{aligned} S &= -\frac{dE}{du}(\mathbf{u}) \\ &= \eta_e(\mathbf{u})F(I(\mathbf{u}), E(\mathbf{u})) \end{aligned}$$

where: u represents the penetration depth of a proton, e(u) is the energy at depth u. $\eta_e(u)$ is the electron density of the material -at depth u- relative to water, and I(**u**) is the mean excitation potential of the object material at depth u.

One should note that the mean excitation potential is similar for most human tissues and maybe replaced by its value for water of the human body(75eV) the function F(I,E) is given by:

$$F(I, E) = K\frac{1}{\beta^2(E)}\left[\ln\left(\frac{2m_ec^2}{I}\frac{\beta^2(E)}{1-\beta^2(E)}\right) - \beta^2(E)\right]$$

where m_ec^2 is the electron rest energy$(511.011keV)$,and $\beta(E)$ is the proton velocity relative to the speed of light c. The constant K is defined as:

$$K = 4\pi u_e^2 m_e c^2 \rho_{e,water} = 0.170\frac{MeV}{cm}$$

where r_e is the classical electron radius $(2.818X10^{-13}cm)$. The relationship between β and E is given by the relativistic relationship:

$$\beta(E) = \sqrt{1 - \left(\frac{E_p}{E + E_p}\right)^2}$$

where $E_p = 938.295MeV$ is the proton rest energy.
Note that the Bethe-Block relationship given by equations above is a non-linear first order differential equation of the function E(u). Since I(u) is usually not exactly known(because the object composition is unknown), integration of this equation is only possible under certain assumptions. For human tissues encountered in proton CT, the variation of I is not very large, and the function F has only a week logarithmic dependence on I. Therefore, it is reasonable to replace I(r) by the mean excitation potential of water, which is 75.0 eV [14]. In this case, F becomes function of E only, and one can separate the terms depending on the variable x (the path variable) and the variable E:

$$\begin{aligned} \int_{x_{in}}^{x_{out}} \eta_e(\mathbf{r})dx &= -\int_{E_{in}}^{E_{out}} \frac{dE}{F(E, I_{water})} \\ &= \int_{E_{out}}^{E_{in}} \frac{dE}{F(E, I_{water})} \end{aligned}$$

Integrating the left side of the equation with respect to the path variable x along a path segment and the right side with respect to the energy between initial energy E_{in} at the beginning of teh path and E_{out} at the end of teh path, we get:

$$\begin{aligned}\int_{u_{in}}^{u_{out}} \eta_e(u)dx &= \int_{E_{in}}^{E_{out}} \frac{dE}{F(E, I_{water})} \\ &= \int_{E_{out}}^{E_{in}} \frac{dE}{F(E, I_{water})}\end{aligned}$$

It is now obvious that the integral of the relative electron density along the proton path can be calculated based on the knowledge of in-and outgoing proton energy. De to the complicated energy dependence of F, the integration should be performed numerically or modeled as a polynomial equation. Also note that the integrated density along the proton trajectory is nothing else than the water-equivalent length of the proton track through the medium [?].

2.2 Simplified version of Bethe-Bloch Equation

By looking at the Bethe-Bloch Equation, and another looking at the given data that we have, I found that it will be helpful to simplify the equation before feeding it to computer program. This will increase performance by reducing the calculation errors, and the time needed to do the calculation.
Here is the a formula derived from Bethe-Block Equation [?]:

$$\begin{aligned}\int_{u_{in}}^{u_{out}} \eta_e(u)dx &= \int_{E_{in}}^{E_{out}} \frac{dE}{F(E, I_{water})} \\ &= \int_{E_{out}}^{E_{in}} \frac{dE}{F(E, I_{water})}\end{aligned}$$

Using a lot of high level math rules and skilles, I could simplify the derived equations to put it in an acceptable shape to be fed to a computer program.
Here is my derived equations

$$\int_{u_{in}}^{u_{out}} \eta_e(u)dx = \int_{E_{out}}^{E_{in}} \frac{dE}{K\frac{(E+E_p)^2}{E^2+2EE_p}\left(\ln\left(\frac{2m_ec^2}{I}\right)\right)}$$

$$\int_{u_{in}}^{u_{out}} \eta_e(u)dx = \int_{E_{out}}^{E_{in}} \frac{dE}{K\frac{(E+E_p)^2}{E^2+2EE_p}\left(\ln\left(\frac{2m_ec^2}{I} + \ln E + \ln E + 2EE_p\right) - \frac{E^2+2EE_p}{(E+E_p)^2} - 2. \ln E - E_p\right)}$$

2.2.1 proof to my simplified version of Bethe-Bloch Equation

Starting from the equation listed in Dr. Schulte's paper [?] we can get:

$$\begin{aligned}\int_{u_{in}}^{u_{out}} \eta_e(u)dx &= \int_{E_{in}}^{E_{out}} \frac{dE}{F(E, I_{water})} \\ &= \int_{E_{out}}^{E_{in}} \frac{dE}{F(E, I_{water})}\end{aligned}$$

but we know that

$$F(I,E) = K\frac{1}{\beta^2(E)}\left[\ln\left(\frac{2m_ec^2}{I}\frac{\beta^2(E)}{1-\beta^2(E)}\right) - \beta^2(E)\right] \tag{2.4}$$

$$K = 4\pi u_e^2 m_e c^2 \rho_{e,water} = 0.170\frac{MeV}{cm} \tag{2.5}$$

where r_e is the classical electron radius ($2.818X10^{-13}cm$). So we can write:

$$\begin{aligned}
\int_{u_{in}}^{u_{out}} \eta_e(u)dx &= \int_{E_{in}}^{E_{out}} \frac{dE}{F(E, I_{water})} \\
&= \int_{E_{out}}^{E_{in}} \frac{dE}{F(E, I_{water})} \\
&= \int_{E_{out}}^{E_{in}} \frac{dE}{K\frac{1}{\beta^2(E)}\left[\ln\left(\frac{2m_ec^2}{I(u)}\frac{\beta^2(E)}{1-\beta^2(E)}\right) - \beta^2(E)\right]}
\end{aligned}$$

but we know that the relationship between β and E is given by the relativistic relationship:

$$\beta(E) = \sqrt{1-\left(\frac{E_p}{E+E_p}\right)^2} \tag{2.6}$$

then

$$\beta^2(E) = 1-\left(\frac{E_p}{E+E_p}\right)^2 \tag{2.7}$$

therefore

$$\int_{u_{in}}^{u_{out}} \eta_e(u)dx = \int_{E_{out}}^{E_{in}} \frac{dE}{K\frac{1}{\beta^2(E)}\left[\ln\left(\frac{2m_ec^2}{I}\frac{\beta^2(E)}{1-\beta^2(E)}\right) - \beta^2(E)\right]}$$

let us concedere$equ_a = \frac{1}{1-\left(\frac{E_p}{E+E_p}\right)^2}$ This can be written as:

$$\begin{aligned}
equ_a &= \frac{1}{1-\left(\frac{E_p}{E+E_p}\right)^2} \\
&= \frac{1}{\left(1-\left(\frac{E_p}{E+E_p}\right)\right)\left(1+\left(\frac{E_p}{E+E_p}\right)\right)} \\
&= \frac{1}{\left(\frac{E_p+E-E_p}{E_p+E}\right)\left(\frac{E_p+E+E_p}{E_p+E}\right)} \\
&= \frac{1}{\left(\frac{E}{E_p+E}\right)\left(\frac{E+2E_p}{E_p+E}\right)} \\
&= \frac{1}{\frac{E^2+2E_pE}{(E_p+E)^2}} \\
&= \frac{(E_p+E)^2}{E^2+2E_pE} \\
&= 1+\frac{E_p^2}{E^2+2E_p}
\end{aligned}$$

therefore

$$\frac{1}{1-\left(\frac{E_p}{E+E_p}\right)^2} = 1+\frac{E_p^2}{E^2+2E_p} \tag{2.8}$$

and from then we can tell that

$$\begin{aligned}
\beta E^2 &= \frac{E^2+2E_p}{(E+E_p)^2} \qquad (2.9) \\
&= \frac{(E+E_p)^2-E_p^2}{(E+E_p)^2} \qquad (2.10) \\
&= 1-\frac{E_p^2}{(E+E_p)^2} \qquad (2.11)
\end{aligned}$$

Now let us conceder $equ_b = \ln\left(\frac{2m_ec^2}{I(u)}\frac{\beta^2(E)}{1-\beta^2(E)}\right)$ therefore: but we know that

$$\begin{aligned}
\ln(a*b) &= \ln(a)+\ln(b) \\
\ln(\frac{a}{b}) &= \ln(a)-\ln(b)
\end{aligned}$$

Therefore:

$$
\begin{aligned}
equ_b &= \ln\left(\frac{2m_ec^2}{I(u)}\frac{\beta^2(E)}{1-\beta^2(E)}\right) \\
&= \ln\left(\frac{2m_ec^2}{I(u)}\frac{1-\frac{E_p^2}{(E+E_p)^2}}{1-\left(1-\frac{E_p^2}{(E+E_p)^2}\right)}\right) \\
&= \ln\left(\frac{2m_ec^2}{I(u)}+\ln\left(\frac{1-\frac{E_p^2}{(E+E_p)^2}}{1-\left(1-\frac{E_p^2}{(E+E_p)^2}\right)}\right)\right) \\
&= \ln\left(\frac{2m_ec^2}{I(u)}\right)+\ln\left(\frac{1-\frac{E_p^2}{(E+E_p)^2}}{\frac{E_p^2}{(E+E_p)^2}}\right) \\
&= \ln\left(\frac{2m_ec^2}{I(u)}\right)+\ln\left(\frac{1}{\frac{E_p^2}{(E+E_p)^2}}-1\right) \\
&= \ln\left(\frac{2m_ec^2}{I(u)}\right)+\ln\left(\frac{(E+E_p)^2}{E_p^2}-1\right) \\
&= \ln\left(\frac{2m_ec^2}{I(u)}\right)+\ln\left(\frac{(E+E_p)^2}{E_p^2}-\frac{E_p^2}{E_p^2}\right) \\
&= \ln\left(\frac{2m_ec^2}{I(u)}\right)+\ln\left(\frac{E^2+2E_pE+E_p^2-E_p^2}{E_p^2}\right) \\
&= \ln\left(\frac{2m_ec^2}{I(u)}\right)+\ln\left(\frac{E^2+2E_pE}{E_p^2}\right) \\
&= \ln(2m_ec)-\ln(I(u))+\ln(E+2E_p)+\ln(E)-2\ln(E_p)
\end{aligned}
$$

Now we apply all that into the Bethe-Bloch Equation which we are working on:

$$
\begin{aligned}
\int_{u_{in}}^{u_{out}}\eta_e(u)dx &= \int_{E_{in}}^{E_{out}}\frac{dE}{F(E,I_{water})} \\
&= \int_{E_{out}}^{E_{in}}\frac{dE}{F(E,I_{water})} \\
&= \int_{E_{out}}^{E_{in}}\frac{dE}{K\frac{1}{\beta^2(E)}\left[\ln\left(\frac{2m_ec^2}{I(u)}\frac{\beta^2(E)}{1-\beta^2(E)}\right)-\beta^2(E)\right]} \\
&= \int_{E_{out}}^{E_{in}}\frac{dE}{\frac{K}{\beta^2(E)}\left[\ln\left(\frac{2m_ec^2}{I(u)}\frac{\beta^2(E)}{1-\beta^2(E)}\right)\right]} \\
&= \int_{E_{out}}^{E_{in}}\frac{dE}{K\frac{(E+E_p)^2}{E^2+2EE_p}\left[\ln(2m_ec)-\ln(I(u))+\ln(E+2E_p)+\ln(E)-2\ln(E_p)-1\right]}
\end{aligned}
$$

Therefore the most simplified version of our equation is

$$\int_{u_{in}}^{u_{out}} \eta_e(u)dx \quad = \quad \int_{E_{out}}^{E_{in}} \frac{dE}{K\frac{(E+E_p)^2}{E^2+2EE_p}\left[\ln(2m_ec) - \ln(I(u)) + \ln(E+2E_p) + \ln(E) - 2\ln(E_p) - 1\right]}$$

for computer simplicity we can do:

$$\int_{u_{in}}^{u_{out}} \eta_e(u)dx \quad = \quad \int_{E_{out}}^{E_{in}} \frac{dE}{K\frac{(E+E_p)^2}{E^2+2EE_p}\left[\ln(\frac{2m_ec}{I(u)} + \ln(E+2E_p) + \ln(E) - 2\ln(E_p) - 1\right]}$$

3. MOST LIKELY PATH DERIVATION

3.1 Introduction and background

The use of protons in medical imaging (proton computed tomography or pCT) is not a new idea (Hanson et al 1982) [15] and has recently gained more relevance due to the growing list of proton treatment centers and the limitations of proton treatment planning based on x-ray imaging (Schaffner and Pedroni 1995, 1998) [29]. One of the disadvantages of pCT is the tendency for protons to scatter in the object by a process called a Multiple-Coulomb Scattering (MCS), thus blurring the image. This disadvantage can be alleviated by measuring the trajectory of individual protons using modern particle detector technology (Klenknecht 1998) [18]. Particle detectors can measure the trajectory of a proton before entering and after leaving the object. However, no direct information is available while the proton is traveling within the object. Therefore, some type of extrapolation is required for optimal spatial resolution in pCT imaging. Because of the random nature of proton scattering, it is not possible to calculate the exact trajectory of the proton within the object. Instead, the most likely path(MLP) along with a probability envelope needs to be calculated.
This chapter presents the theory of the MLP derivation and derives a closed-form expression for the (MLP) when the entrance and exit trajectories are known. Differs from pervious derivations (Schneider and Pedroni 1994, Williams 2004), in that a compact matrix notation are used.

3.2 Multiple-Coulomb Scattering in the Gaussian Approximation

Multiple-Coulomb scattering (MCS) is a physical process that leads to statistical change of the direction of charged particles as they cross matter without changing their total momentum. Most high-energy physicists are familiar with this process since it is often the limiting factor in the performance of charged-particle detectors. A summary of this process can be found in the Review of Particle Physics from the Particle Data Group (Yau 2006) [4]. The most relevant features are described in Williams Paper [29].

MCS is a statistical process involving the sum of many individual elastic interactions between a charged particle and the nuclei of the matter traversed. Each individual nuclear interaction produces a complex distribution of scatter angles. However, after introducing many of these interactions, the combined result is a distribution that is fairly Gaussian. Because Gaussian distributions are simple to deal with, a Gaussian approximation will be assumed in what follows. In this approximation, the amount of MS is characterized by the width σ_θ of the Gaussian characterizing the distribution of scattering angles [29].

3.3 Derivation of the Matrix Form of the Most Likely Path (MLP)

A closed analytical form of the 2D-projected MLP for protons traversing a homogeneous medium when their entry and exit positions and angles are known can be found in the work of Schneider et al [25] and Williams [29]. Here, we will derive a closed analytical form of the MLP using a compact matrix notation, which is advantagous considering the lengthy equations of the previous works.

In the reference system of the proton, its scattering in a material can be described by the two-dimensional vector function

$$y(u) \quad = \quad \begin{pmatrix} \theta(u) \\ t(u) \end{pmatrix} \tag{3.1}$$

at every depth u_1 we can calculate $y(u_1)$ using the same function:

$$y(u_1) \quad = \quad \begin{pmatrix} \theta(u_1) \\ t(u_1) \end{pmatrix} \tag{3.2}$$

where: $t(u_1)$, or t_1 is the lateral displacement. $\theta(u_1)$ or θ_1 is the angle relative to the initial position and direction of the proton at a given depth $u = u_1$. At the boundaries $u = 0$ and $u = u_2$ of the material, $Y_1()$ approaches the values

$$y(u_0) \quad = \quad \begin{pmatrix} \theta(u_0) \\ t(u_0) \end{pmatrix} \tag{3.3}$$

and

$$y(u_2) \quad = \quad \begin{pmatrix} \theta(u_2) \\ t(u_2) \end{pmatrix} \tag{3.4}$$

Note that $t_1 = t(u_1)$ and $\theta_1 = \theta(u_1)$ are statistical variables, which acquire increasing spread with increasing depth. The amount of lateral and angular spread accumulated at depth u1 and the covariance of these quantities can be described by the variance matrix

$$\Sigma_1 \quad = \quad \begin{pmatrix} \sigma^2_{t_1} & \sigma^2_{t_1\theta_1} \\ \sigma^2_{t_1\theta_1} & \sigma^2_{t_1} \end{pmatrix} \tag{3.5}$$

Additional spread is acquired between the depth u1 and the exit depth u2, which can be described by the second matrix

$$\Sigma_2 \quad = \quad \begin{pmatrix} \sigma^2_{t_2} & \sigma^2_{t_2\theta_2} \\ \sigma^2_{t_2\theta_2} & \sigma^2_{t_2} \end{pmatrix} \tag{3.6}$$

In the Gaussian approximation of small angle Coulomb scattering [3], the probability density function of Y1 at depth u1 is given by the bivariate Gaussian [4]

$$
\begin{aligned}
f(y) &= CONST * e^{-y^T.\Sigma^{-1}.y} && (3.7)\\
&= CONST * e^{\chi^2} && (3.8)
\end{aligned}
$$

So we can write the general function as:

$$f(t(u),\theta(u)) = CONST * exp\left(-y(u)^T.\Sigma^{-1}(u).y(u)\right) \qquad (3.9)$$

We have

$$\chi_1^2 = -y_1^T * \Sigma^{-1} * y_1 \qquad (3.10)$$

and

$$\chi_2^2 = -y_2^T * \Sigma^{-1} * y_2 \qquad (3.11)$$

3.4 First step in calculating the most Likely path MLP

As we all know from above

$$\chi^2 = -y^T * \Sigma^* y \qquad (3.12)$$

To do such a multiplication we must first multiply $\Sigma^{-1}(u).y(u)$ let us solve it

$$
\begin{aligned}
\Sigma^{-1}(u)y(u) &= \frac{1}{|\Sigma|}\begin{pmatrix} \sigma_\theta^2 & -\sigma_{\theta t}^2 \\ -\sigma_{\theta t}^2 & \sigma_t^2 \end{pmatrix}\begin{pmatrix} t \\ \theta \end{pmatrix} && (3.13)\\
& && (3.14)\\
&= \frac{1}{|\Sigma|}\begin{pmatrix} \sigma_\theta^2 t - \sigma_{\theta t}^2\theta \\ -\sigma_{\theta t}^2 t + \sigma_t^2\theta \end{pmatrix} && (3.15)
\end{aligned}
$$

Let us now solve for $y_{-T}\Sigma^{-1}(u)y(u)$

$$
\begin{aligned}
y_{-T}\Sigma^{-1}(u)y(u) &= y_{-T}\frac{1}{|\Sigma|}\begin{pmatrix} \sigma_\theta^2 t - \sigma_{\theta t}^2\theta \\ -\sigma_{\theta t}^2 t + \sigma_t^2\theta \end{pmatrix} && (3.16)\\
& && (3.17)\\
&= \frac{1}{|\Sigma|}\left(\sigma_\theta^2 t^2 - \sigma_{\theta t}^2\theta t - \sigma_{\theta t}^2\theta t + \sigma_t^2\theta^2\right) && (3.18)\\
& && (3.19)\\
&= \frac{1}{|\Sigma|}\left(\sigma_\theta^2 t^2 - 2\sigma_{\theta t}^2\theta t + \sigma_t^2\theta^2\right) && (3.20)
\end{aligned}
$$

The most Likely path is located at the most likely area for the same proton.

$$P(t_1, u_1|0,0) \quad = \quad MaxProbability$$

then χ must be very small; therefore

$$0 \quad = \quad -y(u)^T.\Sigma^{-1}(u).y(u)$$

To maximize $f(y)$ we need to make χ a small as possible.
Therefore:

$$\frac{\delta\ \chi^2}{\delta\ \theta}|_{\theta=\theta_0} = 0$$
$$\frac{\delta\ \chi^2}{\delta t}|_{t=t_0} = 0$$

We need to find θ_1, t_1, which satisfies it.

$$\frac{\delta\ \chi^2}{\delta\ \theta}|_{\theta=\theta_0} \quad = \quad \frac{1}{|\Sigma|}\left(2\sigma_t^2 + 0 - 2\sigma_\theta^2 t\right) \tag{3.21}$$

then

$$\theta \quad = \quad \frac{\sigma_{\theta t}^2\theta}{\sigma^2\theta} \tag{3.22}$$
$$\tag{3.23}$$
$$= \quad const_1.t_1 \tag{3.24}$$

$$\frac{\delta\ \chi^2}{\delta t}|_{t=t_0} \quad = \quad \frac{1}{|\Sigma|}\left(2\sigma_\theta^2 + 0 - 2\sigma_t^2\theta\right) \tag{3.25}$$

then

$$t \quad = \quad \frac{\sigma_{\theta t}^2 t}{\sigma^2 t} \tag{3.26}$$
$$\tag{3.27}$$
$$= \quad const_2.\theta_1 \tag{3.28}$$

therefore

$$t = const_2.t_2 = const_2.const_1.t_1 \tag{3.29}$$

means that in one case

$$const_2.const_2 \quad = \quad 1 \tag{3.30}$$
$$\Rightarrow \frac{\sigma_{\theta t}^2}{\sigma_\theta^2}.\frac{\sigma_{\theta t}^2}{\sigma_t^2} \quad = \quad 1 \tag{3.31}$$
$$\Rightarrow \sigma_\theta^2.\sigma_t^2 \quad = \quad \sigma_{\theta t}^4 \tag{3.32}$$
$$\Rightarrow \sigma_\theta^2.\sigma_t^2 - \sigma_{\theta t}^4 \tag{3.33}$$
$$\Rightarrow \sigma_\theta^2.\sigma_t^2 - \sigma_{\theta t}^4 \quad = \quad 0 \tag{3.34}$$

But this case is invalid because we are using $|\Sigma|$ not to be equal to zero. $|\Sigma| = \sigma_{\theta}^2.\sigma_t^2 - \sigma_{\theta t}^4$

therefore finding the most likely path given only the entry position will give us only a straight through line that will result to $\theta = 0$ and $t = 0$

From all the equations above, I can resolute that the gradient ∇ will be given by this equation:

$$\nabla = \begin{pmatrix} \delta\theta \\ \delta t \end{pmatrix} \tag{3.35}$$

$$= 2.\Sigma^{-1}.y \tag{3.36}$$

to find the most likely path we look at the entrance and the exiting proton trajectories for points approaching the corresponding target surfaces [29]

First we consider the entry proton trajectory to be the value at y_1 so we need to find $f(t_2, \theta_2 | t_1, \theta_1)$. Let us assume that $\theta^{`} = \theta_2 - \theta_1$.

Then we can do our coordinate transformation

$$\begin{matrix} u_2^{'} \\ t_2^{'} \end{matrix} = \begin{pmatrix} \cos\theta_1 & \sin\theta_1 \\ -\sin\theta_1 & \cos\theta_1 \end{pmatrix} \begin{pmatrix} u_2 - u_1 \\ t_2 - t_1 \end{pmatrix} \tag{3.37}$$

therefore we get

$$u_2^{'} = \cos\theta_1(u_2 - u_1) + \sin\theta_1(t_2 - t_1) \tag{3.38}$$

$$t_2^{'} = -\sin\theta_1(u_2 - u_1) + \sin\theta_1(t_2 - t_1) \tag{3.39}$$

3.4.1 The Angel Approximation method to find the solution

when sin is very small then we can ignore it and cos will be equal to θ therefore

$$u_2^{'} = u_2 - u_1 \tag{3.40}$$

$$t_2^{'} = -\theta_1(u_2 - u_1) + (t_2 - t_1) \tag{3.41}$$

so that we will have a new function f_2 which can be given as $f(t_2^{'}, \theta_2^{'} | t_1^{'}, \theta_1^{'} = const. \exp(-y_2^{'T}\Sigma_2^{-1}y_2^{'})$ as $\chi_2^2 = -y_2^{'T}\Sigma_2^{-1}y_2^{'}$

and $y_2^{'} = \begin{matrix} t_2^{'} \\ \theta_2^{'} \end{matrix}$

also $\Sigma_2 = \begin{matrix} \sigma_{2t}^2 & \sigma_{2\theta t}^2 \\ \sigma_{2\theta t}^2 & \sigma_{2t}^2 \end{matrix}$

Here is another way of thinking about the problem:
According to Bay's Theorem [28] we found the following:

$$P(y_1|y_2) = \frac{P(y_2|y_1)P(y_1)}{P(y_2)} \tag{3.42}$$

we could write our equation using Bay's theorem: and using our old equations to find the following:
$\chi_2^{'2} = -y_2^{'T} \Sigma_2^{-1} y_2^{'}$
which is equal to:
$\chi_2^{'2} = \chi_1^1 + \chi_2^2$

Since we know that:

$$\begin{aligned} u_2^{'} &= u_2 - u_1 & (3.43) \\ t_2^{'} &= -\theta_1(u_2 - u_1) + (t_2 - t_1) & (3.44) \end{aligned}$$

Let us define

$$\begin{aligned} f_1(t_1, \theta_1) &= t_1 & (3.45) \\ f_2(t_1, \theta_1) &= \theta_1 & (3.46) \\ f_1(t_2, \theta_2) &= -\theta_1(u_2 - u_1) + (t_2 - t_1) & (3.47) \\ f_2(t_2, \theta_2) &= \theta_2 - \theta_1 & (3.48) \\ & & (3.49) \end{aligned}$$

3.4.2 The exact solution of the MLP problem

Given $y_1 = \begin{bmatrix} u_1 \\ t_1 \\ \theta_1 \end{bmatrix}$ which describes the parameter vector of the proton at depth u_1, and $y_2 = \begin{bmatrix} u_2 \\ t_2 \\ \theta_2 \end{bmatrix}$ which describes the known parameter vector at the exit location, the solution for y_1 that minimizes $\chi^2 = \chi_1^2 + \chi_2^2$ where:

$$(3.50)$$

$$\chi^2 = y_1^T \begin{bmatrix} 0 & 0 \\ 0 & \Sigma_1^{-1} \end{bmatrix} y_1 + \quad (3.51)$$

$$y_2^{\prime T} \begin{bmatrix} 0 & 0 \\ 0 & \Sigma_2^{-1} \end{bmatrix} y_2^{\prime} \quad (3.52)$$

where

$$y_2^{\prime} = \begin{bmatrix} Q_{\theta_1} & 0 \\ 0 & 1 \end{bmatrix} (y_2 - y_1) \quad (3.53)$$

and

$$Q_{\theta_1} = \begin{bmatrix} \cos\theta_1 & \sin\theta_1 \\ -\sin\theta_1 & \cos\theta_1 \end{bmatrix} \quad (3.54)$$

will be given as:

$$MLP = -\begin{bmatrix} 0 & 0 \\ 0 & \Sigma_1^{-1} \end{bmatrix}^{+} \frac{dy_2'}{dy_1} \begin{bmatrix} 0 & 0 \\ 0 & \Sigma_2^{-1} \end{bmatrix} y_2' \tag{3.55}$$

where

$$\frac{dy_2'}{dy_1} = \begin{bmatrix} 0 \\ 0 \\ R_{\theta_1}(y_2 - y_1) \end{bmatrix} - \begin{bmatrix} Q_{\theta_1} & 0 \\ 0 & 1 \end{bmatrix} \tag{3.56}$$

and

$$\begin{aligned} R_{\theta_1} &= \frac{dQ_{\theta_1}}{d\theta_1} && (3.57) \\ &= \begin{bmatrix} -\sin\theta_1 & \cos\theta_1 \\ -\cos\theta_1 & -\sin\theta_1 \end{bmatrix} && (3.58) \end{aligned}$$

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