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A Simulation Based Approach for Detection of Cataract and Retinitis Pigmentosa using Protein Secondary Structure

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Abstract - Proteins are the basis of all organisms. Abnormality on any part of the human body can easily be detected by referring to the protein structure on that particular part. To determine any deformation in the protein structure different experimental techniques are used. Alpha-crystallin is a protein found in the eye-lens which is responsible for formation of cataract and Peripherin-2 is the protein found in the photoreceptor cells and any deformation in this protein is responsible for formation of Retinitis Pigmentosa. This paper investigates the encoding efficiency of alpha-crystallin and peripherin-2 using a coding scheme. The system used here at first detects the chemical components which are the basis of amino acids and then detects the amino acids which in turn are the basis of proteins. The system finally recognizes the alpha-crystallin and peripherin-2 proteins and the changes that occur in the chemical structure of alpha-crystalline and peripherin-2 during cataract and retinitis pigmentosa using secondary structure of proteins.

Keywords - Alpha-crystallin, Peripherin-2, Cataract, Retinitis Pigmentosa.

1. INTRODUCTION

Blindness or serious vision impairment is one of the most feared disabilities known to mankind. Two most common vision impairments are- Cataract and Retinitis Pigmentosa. Onset of eye lens opacification commonly known as "Cataract" is a common disease of human eye. Cataract detection is a problem related to the biomedical field which deals with the detection and analysis of opacity in the crystalline lens of the eye [1]. Cataracts are the single biggest cause of blindness and are responsible for almost half of all cases worldwide.

Retinitis pigmentosa is a clinically and genetically heterogeneous group of hereditary disorders in which there is progressive loss of photoreceptor and pigment epithelial function. It causes severe vision impairment and often blindness. Symptoms like difficulty in night vision (night blindness), no central vision, blurry vision, poor color separation and extreme tiredness are experienced by people suffering from retinitis pigmentosa will experience. In addition, RP can be accompanied by cataract, open-angle glaucoma, refractive errors, keratoconus, optic nerve head drusen and cystoid macular oedema.

2. BASIC BIOLOGICAL CONCEPTS

2.1 History:

In our work we tried to detect Cataract and RP by analyzing the protein structure. So we are emphasizing on different types of protein structures.

Basically proteins have four different structures.

- Primary: Unique sequence of aminoacids, biological information unit that determines the structure and function of a protein.
- Secondary: Locally defined spatial arrangement and regularities of aminoacids with respect to one another. The three secondary structures are- alpha helix, beta sheets and coil or loop which are influenced by the properties of each aminoacids.
- Tertiary: Three dimensional structures which are responsible for the functional characteristics of proteins.
- Quarternary: Composed of two or more subunit of tertiary structures.

The secondary structure has 3 regular forms and they are-

- Helical: It is the classic element of protein structure which would be stable and energetically favorable in proteins.
- Extended beta sheets: It is the second major structural element found in globular proteins whose structure is built up from a combination of several regions of the polypeptide chain.
- Loop or Reverse Turns or Coils: Most protein structures are built up from combinations of secondary structure elements, alpha helices and beta strands which are connected by loop regions of various lengths and irregular shape.[2]

A combination of the secondary structure elements forms the stable hydrophobic core of the molecule and the loop regions are at the surface of the molecule [2]. Theoretically it is not possible to predict protein structures with 100% accuracy because of the fact that there are 20 different aminoacids and thus ways to generate similar structures in proteins by different aminoacids is much more.

From the detailed survey of different literatures it is observed that mutations in the alpha-crystallin and

peripherin-2 gene are responsible for formation of Cataract and Retinitis Pigmentosa respectively. The eye lens is composed of water (65%) and protein (35%). There are two types of protein in the eye lens. One is insoluble protein known as albuminoid and the other is soluble protein consist of α, β and γ crystallines [3]. Cataract is caused by crystalline aggregation and can be recognized by periodic measurement of the crystalline dimensions. As a person ages, there is a loss of *α*-crystallins, which diminishes the capacity of the lens to prevent uncontrolled protein aggregation due to the irreversible binding of damaged proteins and the fact that most of the lens lacks the capacity to synthesize new proteins. Thus, a measure of the *α*-crystallin remaining in the lens may reflect the level of protective reserve and finally detecting the presence of opacities in the lens[4].
Retinitis Pigmentosa is a very serious hereditary disorder. A method named Electroretinography is used primarily for the diagonosis of retinitis pigmentosa. Retinitis pigmentosa can run in families. The disorder can be caused by a number of genetic defects. The cells controlling night vision (rods) are most likely to be affected. However, in some cases, retinal cone cells are damaged the most. The main sign of the disease is the presence of dark deposits in the retina. This disease is primarily due to the X linked manner autosomal gene which is dominant in male. Therefore males are affected mostly by this disease [5]. RP can lead to several other complications like cystoids macular edema [6]. Till date there is no significant technique for curing this disease permanently. But it may be controlled or slow down by the antioxidants such as high dosage of vitamin A. Again it has side effects such as taking high dosage of vitamin A causes serious liver problem. So technique for treatment of this blindness is still an ongoing research. The mode of inheritance of retinitis pigmentosa is determined by family history. Management of RP is very difficult because there are no proven methods of treatment [7].

2.2 Formation Of Cataract And RP

The eye is one of nature's complex wonders. The human eye is an organ which reacts to light for several purposes. As a conscious sense organ, the mammalian eye allows vision. There are several fatal eye diseases based on protein synthesis like Cataract, Stargardt disease, Choroideremia, Oguchi disease, Vitelliform Mascular Dystrophy, Retinitis Pigmentosa etc. Out of all these diseases, Cataract is the most common vision impairment and is responsible for almost half of the cases worldwide. It is a clouding or loss of transparency of the lens in the eye as a result of tissue breakdown and protein clumping. Retinitis pigmentosa is the most common hereditary disorder which causes progressive loss of vision.
The basic biological concepts behind the formation of these two diseases are described below.

2.2.1 Cataract

- Formation of cataract in human eye: The basis behind the formation of cataract is the clumping of the eye lens protein. When beta and gamma-crystallins and other cellular proteins in the lens are damaged by oxidative stress, they unravel from the tip. They become sticky and begin attaching themselves to other proteins. Alpha-crystallin plugs up the unraveling tips and prevents the molecules from aggregating further. As a result, the lens remains stable and remains clear.
- Alpha Crystallin factor: Alpha crystallin is a molecular chaperone which prevents other proteins from aggregating. There are two α-crystallin genes; Alpha-A and Alpha-B.

  a) Alpha-A: It is mainly found in the eye-lens. In humans, the alpha-A gene encodes for a 173 aminoacids residues polypeptide. It contributes to the transparency and refractive index of the lens. The aminoacids sequence of Alpha-A crystallin is as given as:
  MDVTIQHPWFKRTLGPFYPSRLFD
  QFFGEGLFEYDLLPFLSSTISPYYR
  QSLFRTVLDSGISEVRSDRDKFVIF
  LDVKHFSPEDLTVKVQDDFVIHG
  KHNERQDDHGYTSREFHRRYRLP
  SNVDQSALSCSLSADGMLTFCGPK
  IQTQLDATHAERAIPVSREEKPTSA
  PSS.

  b) Alpha-B: It is essentially a ubiquitous protein and is a bona fide member of the small heat-shock protein family. Alpha-B gene encodes for a 175 aminoacids residues polypeptide and have chaperone like activity. Similarly, the aminoacids sequence of Alpha-B crystallin is given as:
  MDIAIHHPWIRRPFFPFHSPSRLFD
  QFFGEHLLESDLFPTSTSLSPFYLR
  PPSFLRAPSWFDTGLSEMRLEKDR
  FSVNLDVKHFSPEELKVKVLGDVI
  EVHGKHEERQDEHGFISREFHRKY
  RIPADVDPLTITSSLSSDGVLTVNG
  PRKQVSGPERTIPITREEKPAVTAA
  PKK
  Where M represents the aminoacid Methionine, D is Aspartic acid, V is valine, T is Threonine, I is Isoleucine and so on.

2.2.2 Retinitis Pigmentosa

- Formation of Retinitis Pigmentosa (RP7) in human eye: The basis behind the formation of retinitis pigmentosa is the opacities present in the rod and cone cells of the eye or in the retinal pigment epithelium. Affected individuals may experience defective light to dark, dark to light adaptation or nyctalopia (night blindness), as the result of the degeneration of the peripheral visual field (known as tunnel vision).

Sometimes, central vision is lost first causing the person to look sidelong at objects [8].

- Peripherin 2 factor: Peripherin-2 is a protein, that in humans is encoded by the PRPH2 gene. Peripherin-2 is found in the rod and cone cells of the retina of the eye. In humans, the PRPH2 gene encodes for 173 amino acids residues polypeptide. The aminoacids sequence is as follows:
  MALLKVKFDQKKRVKLAQGLWLMNWFS
  VLAGIIIFSLGLFLKIELRKRSDVMNNSESHF
  VPNSLIGMGVLSCVFNSLAGKICYDALDPA
  KYARWKPWLKPYLAICVLFNIILFLVALCC
  FLLRGSLENTLGQGLKNGMKYYRDTDTPG
  RCFMKKTIDMLQIEFKCCGNNGFRDWFEIQ
  WISNRYLDFSSKEVKDRIKSNVDGRYLVD
  GVPFSCCNPSSPRPCIQYQITNNSAHYSYDH
  QTEELNLWVRGCRAALLSYYSSLMNSMG
  VVTLLIWLFEVTITIGLRYLQTSLDGVSNPE
  ESESESEGWLLEKSVPETWKAFLESVKKLG
  KGNQVEAEGAGAGQAPEAG
  Where each letter represents amino acids. For example, M represents the aminoacid Methionine, D is Aspartic acid, V is valine, T is Threonine, I is Isoleucine and so on.

3. METHODOLOGY

In this paper, a classifier has been designed which can detect the abnormality in the chemical structure of alpha-crystallin and peripherin-2 protein which happens during Cataract and Retinitis Pigmentosa (RP7). It consists of the following steps:

3.1 Selection of Data

In our work we have considered the proteins alpha-crystallin and peripherin-2. Alpha-crystallin consists of two sub units: Alpha-A and Alpha-B consisting of 173 and 175 aminoacids residues respectively and peripherin-2 encodes for 346 aminoacids residues polypeptide. Amino acids are the essential medium through which the human gene translates into proteins. Primarily there are 20 amino acids but in addition to these 20 aminoacids, there are some other amino acids found in the human body but they are not constituents of proteins [9]. The chemical components that form the basis of these aminoacids are carbon, hydrogen, oxygen, nitrogen and sulphur. Each amino acid has a carboxyl group (COOH) and an amine group (NH2), a hydrogen atom and a specific side chain (R-group) bonded to the same carbon atom which is named as α carbon atom. These 20 aminoacids are the inputs to the first system.

3.2 Generation of the Coding Scheme

Based on the chemical structure of aminoacids, a coding scheme is generated to detect the proteins alpha-crystallin and peripherin-2. Unique BCD codes are used for coding each component or symbol in the chemical structure of these aminoacids. Considering the chemical components, each of the components is coded using the generated coding scheme. These codes are then given to system I as input. Then the 20 amino acids are coded with the help of the coded chemical structure based on their hydrophobic and hydrophilic indexes using system II. Then the considered proteins are coded with the help of coded amino acids using system III. The system model shown in Fig 3 comprises of four systems for detection. The first system (System I) uses the chemical components as inputs and provides their necessary coding. The second system (System II) provides the identification of the aminoacids. The third system (System III) uses the coded aminoacids as inputs and detects alpha-crystallin and peripherin-2 protein. The primary structures of the proteins from the 3rd classifier is given to the fourth system (System IV) as input which classifies the 3 secondary structures-alpha helix, beta sheets and coil or loop. The final structure is derived from the majority selection of the 3 secondary structures.

3.3 System Design and Implementation

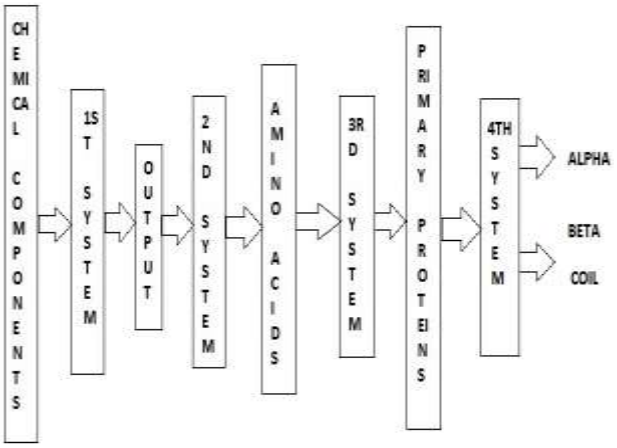

Fig 3: System Block Diagram

The entire work may be summarized by the following steps-

- Extracting and coding the chemical components present in the aminoacids.
- Extracting the chemical structure of the aminoacids.
- Coding the aminoacids.
- Extract the aminoacid sequence of primary proteins.
- Detecting the proteins.
- Predicting their secondary structures.

4. RESULTS

The following figures represents the performance of the proteins Alpha-A, Alpha-B and Peripherin in percent where the blue color represents the percentage of alpha-helix, green color represents the beta sheets and the red color represents the loops. Figure (a), (b) and (c) represents performance of Alpha-A, Alpha-B and

Peripherin-2 without cataract and retinitis pigmentosa respectively. From the figures we can conclude that for all the three proteins when there is no cataract and RP7 in the eye lens they have alpha as the secondary structure. Certain structural changes occur in the protein sequence when a person suffers from cataract as well as retinitis pigmentosa-7(RP7). Figure (d), (e) and (f) represents the percentage of alpha-crystallin and peripherin-2 during cataract and RP7 respectively. From the figures we can conclude that during cataract and retinitis pigmentosa all the three proteins are found with alpha secondary structure in the eye lens.

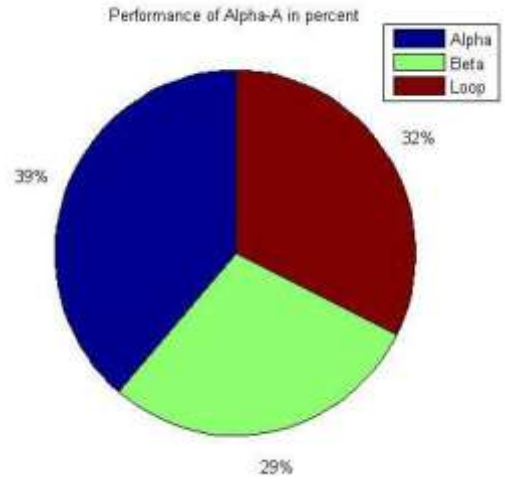

Fig (a) Performance of Alpha-A

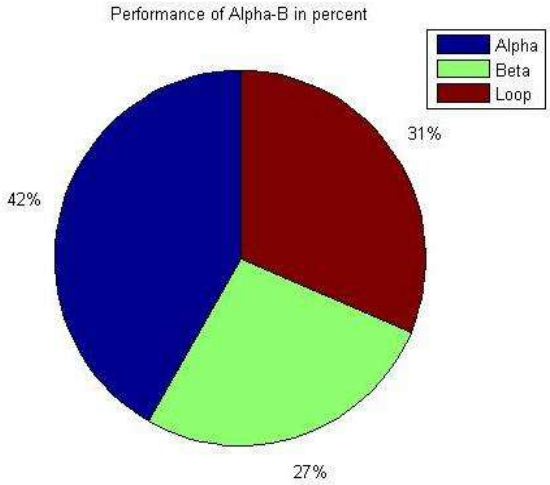

Fig (b) Performance of Alpha-B

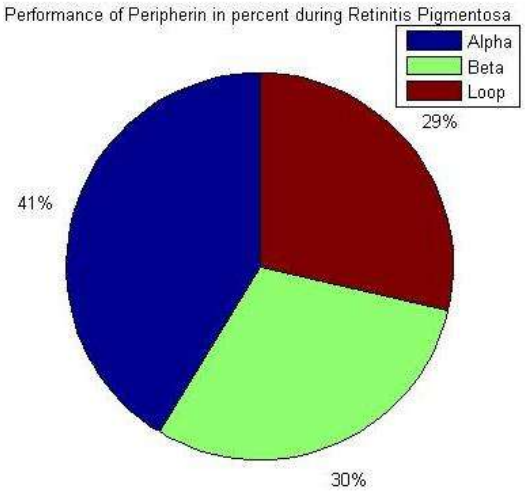

Fig (c) Performance of Peripherin-2

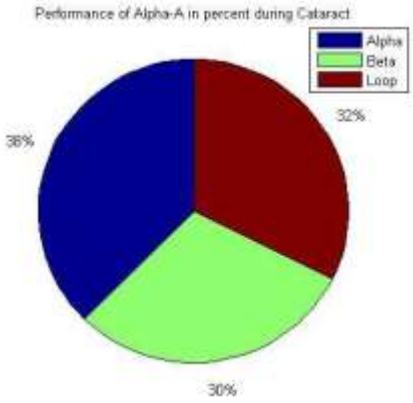

Fig (d) Performance of Alpha-A during Cataract

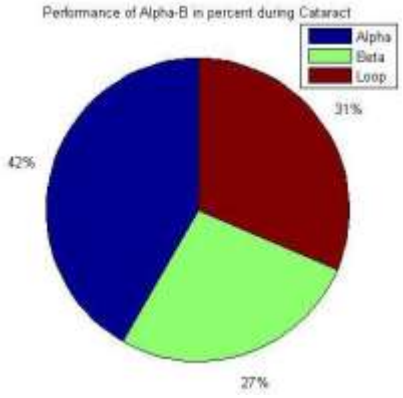

Fig (e) Performance of Alpha-B during Cataract

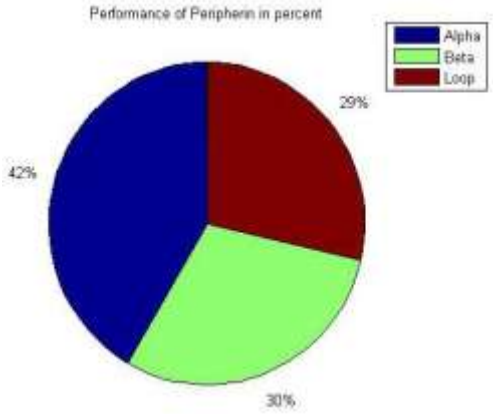

Fig (f) Performance of Peripherin-2 during RP7

We have compared the results of our proposed work with that of Protein Data Bank(PDB) and Chou-Fasman servers[10] and it shows similarity with both the results of PDB and Chou-Fasman. The following tables shows the comparison of the results of our proposed system with the PDB Database and the Chou-Fasman server.

Table 1: Comparison of Proposed System with the other Methods for normal proteins

Protein Name	Proposed System Results	PDB Results	Chou-Fasman Results
Alpha-A	Alpha	Alpha	Alpha
Alpha-B	Alpha	Alpha	Alpha
Peripherin-2	Alpha	Alpha	Alpha

Table 2: Comparison of Proposed System with the other Methods for proteins with abnormalities.

Protein Name	Proposed System Results	PDB Results	Chou-Fasman Results
Alpha-A	Alpha	Alpha	Alpha
Alpha-B	Alpha	Alpha	Alpha
Peripherin-2	Alpha	Alpha	Alpha

It is seen that the results obtained for alpha-crystallin (alpha-a and alpha-b) and peripherin-2 from our proposed work for both in normal state and in presence of abnormalities during cataract and RP7 respectively are same. Both of the proteins has alpha as their secondary structures in both the states. Thus we can conclude that it is not possible to detect cataract and RP7 by predicting the secondary structure of proteins.

5. Conclusion

This work shows a simulation based approach to detect the eye-lens proteins alpha-crystallin and peripherin-2 using protein synthesis. The first system is configured to handle different coded values of the chemical components. The second system identifies the amino acids and the third system recognizes the proteins alpha-crystallin and peripherin. The fourth system determines the secondary structures. These four systems are based entirely on the coding of the proteins and the coding scheme is again based on each and every amino acid and the chemical components present in their chemical structure. As it covers all the components of the aminoacid sequence therefore the accuracy level is very high in this case.

Cataract is the most common vision impairment known to mankind and Retinitis pigmentosa is a very serious genetic disease. Once cataract has been developed there is no other option except the surgical removal of the impaired lens with an intra-ocular lens. However several complications may occur during the surgery. Retinitis pigmentosa is also the most common hereditary disorder and currently there is no cure for this disease. So by synthesizing alpha-crystallin and peripherin-2 proteins which are responsible for these dreadful diseases, preventive measures can be taken in the embryonic stage. Only continued perseverance in the research can contribute a better accuracy in the detection.

The ease with which this simulation based approach provides the detection of the proteins-alpha crystalline and peripherin-2 makes it possible for similar applications. The success rate achieved in the detection makes the proposed approach reliable means of study of the proteins and can be extended to include more known and unknown sequences of proteins related to several eye-diseases which will make it a reliable setup for research in the near future.

6. References

[1] Joseph Horwitz,:Review on Alpha-Crystallin. Experimental Eye Research, pages 145–153, (2007)

[2] Pronami Bora and Hemashree Bordoloi : A Simulation Based Approach For Detection of Retinitis Pigmentosa Based On Protein Synthesis. IJCA Vol-66, March 2013.

[3] Branden, C.; and Tooze, J. : Introduction to Protein Structure.

[4] Brown, N.,Harding, J.;Bron, A.;Sparrow, J; Blakytny, R . : The Lens In Diabetes. vol. 7, pages 260–275, (1993).

[5] Rafat R Ansari, and James King.,:Ocular static and dynamic light scattering. A noninvasive diagnostic tool for eye research and clinical practice. Journal of Biomedical Optics, pages 22–37,(2004).

[6] Pete Humphries and Avril Kennan, : Light in Retinitis Pigmentosa. Review Article Trends in Genetics, vol. 21, pages 103–110, (2005)

[7] Christian Hamel, : Retinitis Pigmentosa. Orphanet,(2003).

[8] Berson, EL: Retinitis pigmentosa. The Friedenwald lecture. Invest Ophthalmol Vis Sci 34:1659–1676, (1993).
[9] J Heckenlively,:The frequency of posterior subcapsular cataract in the hereditary retinal degenerations. Am J Ophthamol, pages 733–738(1987)
[10] Zaman Choudhary, Lin, K.; Neill,;The Significance and Relationships of Amino Acids and Protein in Chronic Disease and General Wellness. Immune System Management Inc. rev 2, July(2002).
[11] O Edholm, :The Chou-Fasman method for predicting secondary structure. Advanced Networks Research Group, School of Information Technologies, pages 83–87, (2008)
[12] R Augusteyn and J Korentz : A Possible Structure of Alpha-Crystallin. Elsevier Science Publishers B. V. (Biomedical Division)Federation of European Biochemical Societies, (1987).
[13] Matthew J Betts, Russell, R: Amino Acid Properties and Consequences of Substitutions. Bioinformatics for Geneticists, vol. 2, (2003).
[14] D Nelson and M Lehninger: Principles of Biochemistry.
[15] Fishman, M.; Maggiano, JM: Foveal lesions seen in retinitis pigmentosa. Arch Ophthalmoly, (1999).

Weblinks

1. http://www.ncbi.nlm.nih.gov/pubmedhealth/s/diseases_and_conditions/
2. https://www.google.co.in/url?sa=t&rct=j&q=&esrc=s&source=web&cd=4&cad=rja&ved=0CGAQFjAD&url=http%3A%2F%2Fwww.medicinenet.com%2Fretinitis_pigmentosa%2Farticle.htm&ei=1HexUZLbCsSIrAejmIH4DA&usg=AFQjCNF8KaUshM4xL8027lnUMFmt3a6g&sig2=pEGyiRrdjZXIqyXcVjiXqQ&bvm=bv.47534661,d.bmk