

Significance of the Theoretical Concept of “Gene Maturation Clock” and Attempts to Further Clarify it

Santhoshkumar, R.

Post Graduate Department of Botany
N.S.S. College, Pandalam, Pathanamthitta, Kerala, India
(Affiliated to University of Kerala, Thiruvananthapuram, Kerala, India)

This article is distributed under the Creative Commons by-nc-nd Attribution License.
Copyright © 2022 Hikari Ltd.

Abstract

This article explains the merits and significance of the “gene maturation clock”. In addition an attempt is made to resolve the complexities and confusions of the original article. This includes “0” to “100% clockwise direction”, “100” to 0% anticlockwise”, “silent condition” and “On” and “Off” conditions. The resulting features of these four conditions are described in great detail here. The previous article explained that when a clockwise movement occurs (when a gene moves from 0 percent to 100 percent) a particular quality increases over time. The article goes on to say that this is a positive movement in living things. But this article tries to explain that this kind of movement is not always good for living things. The second condition is that a specific quality decreases over time when an anticlockwise movement occurs (when a gene moves from 100 percent to Zero percent). The article goes on to say that this is a negative movement in living things. But this article tries to explain that this kind of movement is not always negative for living things. The third condition is the silent condition. This only happens after a particular character has reached one hundred percent. This is, if the gene continues to move clockwise even after reaching 100%, it will go directly 0%. As a result, that particular trait disappears very quickly from a person. Fourth, the article describes two situations, *i.e.* “On” and “Off” conditions. Both of these situations will be after a particular character reaches one hundred percent. If the gene transfer takes place in the “Off” state, that particular trait

will not be passed on to the next generation. But if the gene is passed on in the “On” state, that particular trait can be passed on to the next generation. But overtime, that particular trait is likely to diminish. This article describes it in great detail. All four of these conditions can be experienced as good or bad in individuals in one way or another. That is, the outcome depends on the “behaviour” that can be transmitted. With this theory, we can understand how much a person’s behavior will change in the future. More precisely, if we observe the previous two or three generations of person, we can know for sure whether a trait that existed in that person at that time will increase or decrease. An example of this is the ability of the father of a famous singer to sing and the different abilities of his two children. The famous singer is more talented than his father, but one of his two sons sings well, but the other son does not want to sing. This article explains the reasons for these differences. Furthermore, the section describing the significance of this article in detail and it relates to a person’s life.

Keywords: Gene Maturation Clock, Clockwise, Anticlockwise, Paradoxical, “Off” condition, “On” condition, “Silent” condition

Introduction

This article is intended to dispel some of the doubts raised in the previous article⁽⁷⁾. The advantages of the new concept are further explained in the previous article. But this article tries to explain its advantages and disadvantages accurately. To that end, all the situations described in the previous article will be described again. This is the first time such as idea has been applied to the Science. Therefore, some accuracy is required. So if you read this article in its entirety, you will clear up all the doubts of the pervious article and understood exactly what it says. This was the first attempt to elucidate this type of variation in an individual’s genes. But some other studies have tried to explain some other features and changes in genes^(1, 2,3,4, 5.). But most of the studies did not try to explain the pattern human behavioral^(6, 8, 9, and 10). So the present article entitled “A Concept of Gene maturation Clock” Is it real? was a new concept incorporated into the Science.

What was the basis of the concept of the previous article?

The question was whether genes, like all living thing, would pass through childhood, adolescence, and old age⁽⁷⁾. It was from that thought that this new idea emerged. For that, the biographies of talented individuals from different walks of life were examined. Some of them are famous in music, some in teaching, some in research, and some in politics. Since then, information on several generations of such individuals has been collected. The important thing that emerges from this observation is that a particular quality is felt to vary greatly from one generation to

the next. That is, when a particular quality is passed down from one generation to the next, it increases or decreases.

Result and Discussion

It gave two examples to complete the pervious theoretical article. In this article describes those examples once again. Three conceptual diagrams are used for the completeness of this article. These conceptual diagrams are represented in this article as Figure 1, Figure 2, and Figure 3.

Example 1

The first example mentioned in that article is about a famous singer. For that, information on three generations of that person was collected. The father (it is considered the first generation in this study) of this famous singer (it is considered the second generation in this study) was a singer, but he was not so famous. One of the two children (it is considered the third generation in this study) of the famous singer want to sing but could not be as famous as his father and the second son (is also considered the third generation in this study) does not want to sing.

Example 2

The second example mentioned in that article is about a famous painter. For that, information on four generations of that person was collected. The father (it is considered the first generation in this study) of this famous painter (it is considered the second generation in this study) was painter, but he was not so famous. The next generation (it is considered the third generation in this study) of the famous painter want to painting. But this generation wanted to paint, but could not become as famous as previous generations. The fourth generation is not interested in painting.

These two examples are described in the previous article. The concept of “Gene Maturation Clock” was formulated based on these examples. For the sake of accuracy; almost everything mentioned in the previous article is explained once again in this article.

Differences in traits from one generation to the next: a theory based on its causes

The previous article explained that there can be a lot of differences in genes. A conceptual diagram is given in the previous article. This figure has been copied to this article for completeness. In that article uses a special number system. The first figure of the previous article describes four possibilities, two of which are obvious and two which are indirect. The following are the four situations described in the original article based on the first figure (figure 1). For the sake of completeness of this article, it explained here once again.

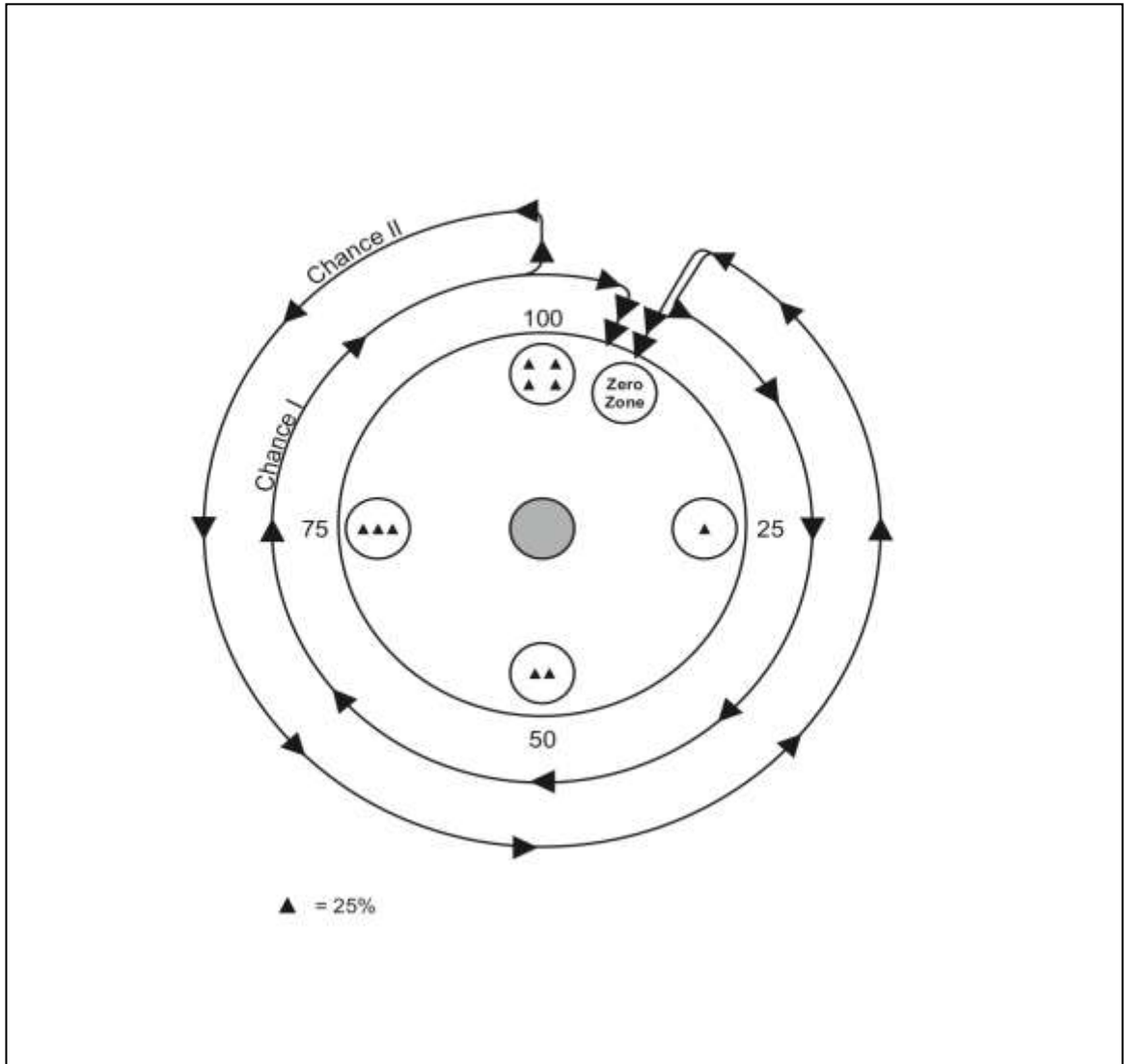


Figure 1. Showing movement of gene in clockwise and anti-clockwise direction (Gene Maturity Clock) (Source: Santhoshkumar,R., 2021) (Conceptual diagram)

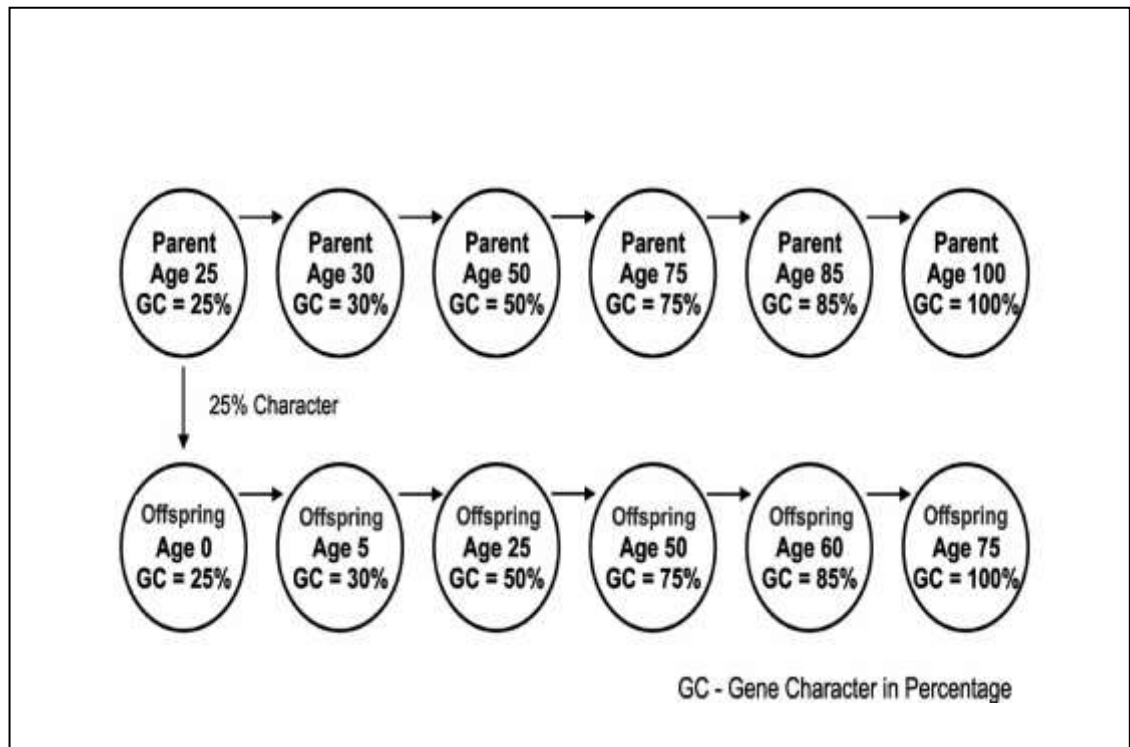


Figure 2. Showing an increasing trend in a particular character/trait or quality of genes (if moving in clockwise direction): GC–Gene character in percentage (Source: Santhoskumar R., 2021) (Conceptual diagram).

Additional description for figure 2: According to the new concept, a person’s age is 25 and the gene quality for a particular trait is 25%. At the age of 25, the person gave birth to a child. At this time the age of the offspring was zero, but the quality of the specific gene trait in the offspring was 25%. This is because the quality of gene controlling the particular trait reaches 25% of the parent and is passed directly from the parent to offspring. After that the age of the parent increases to 30 and in parallel his gene quality increases to 30%. At the same time the age of his offspring is 5; but the quality of genes has increased to 30%. These changes up to the parent’s age of 100 are clearly given in this figure. Age of parent is 100 while age of offspring is 75. However, the gene quality is 100 in both parent and offspring. Changes in gene quality over two generations are only explained in this figure. The quality of genes before and after these two generations is not included in this figure. The quality of the gene trait starts before these two generations and gradually increase and can be maximized in the third generation (offspring is considered the third generation in this figure). After achieving 100% quality it may go “Anti-clockwise”, “Silent”, “On” or “Off” states. Parallel changes occur in parent and offspring regardless of age.

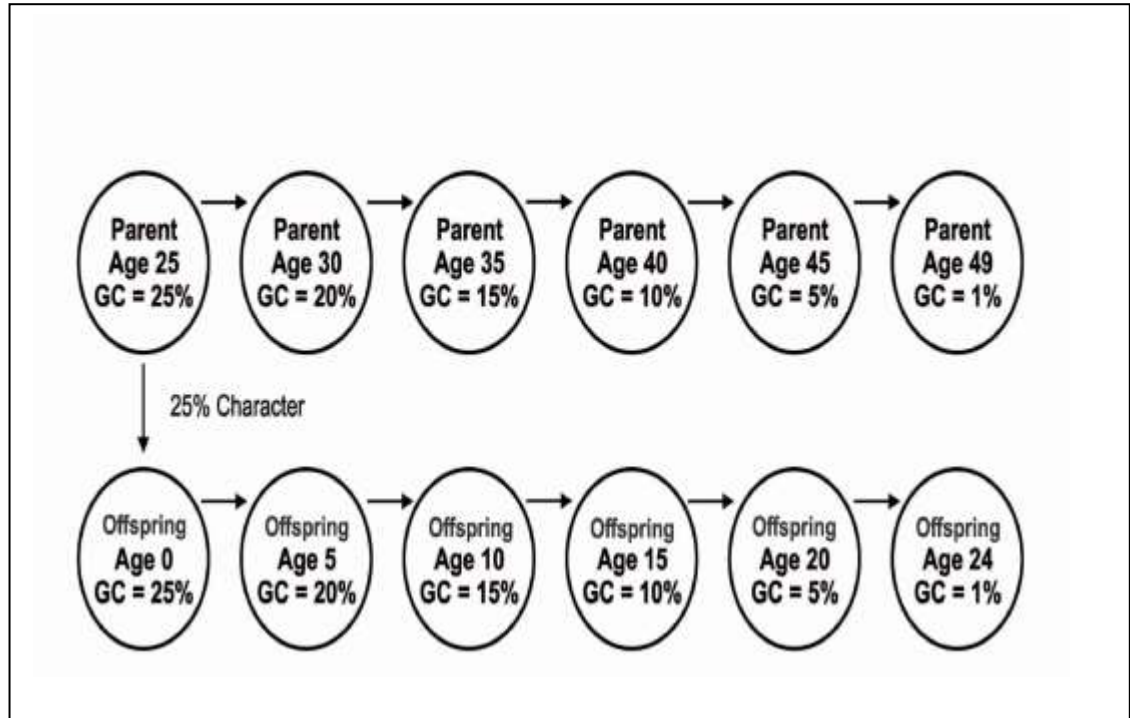


Figure 3. Showing a decreasing trend in a particular character/trait or quality of genes (if moving in an anti-clockwise direction). Same time some other characters may go clockwise direction (But not included in the diagram).Source: Santhoshkumar, R. 2021 (Conceptual diagram).

Additional description for figure 3: According to the new concept, a person's age is 25 and the gene quality for a particular trait is 25%. At the age of 25, the person gave birth to a child. At this time the age of the offspring was zero, but the quality of the specific gene trait in the offspring was 25%. This is because the quality of gene controlling the particular trait reaches 25% of the parent and is passed directly from the parent to offspring. After that the age of the parent increases to 30 and in parallel his gene quality decreases 20%. At the same time the age of his offspring is 5; but the quality of genes has decreased to 20%. These changes up to the parent's age of 49 are clearly given in this figure. Age of parent is 49 while the age of offspring is 24. The subsequent changes after parental age of 49 are not included in this figure. Changes in gene quality over two generations are only explained in this figure also. The quality of genes before and after these two generations is not included in this figure. The quality of the gene trait starts before these two generations and gradually decreases and can be minimized in the third generation (offspring is considered the third generation in this figure). After reaching the 1% level it may move "clockwise" again, or it may go "Silent", "On" or "Off" states. Parallel changes occur in parent and offspring regardless of age.

Chance 1: Clockwise movement of a gene that regulates a particular trait; *i.e.* 1% to 100%

The original article explained that this is a good movement helps to improve the quality of a particular trait or gene in an organism over time (figure 2). In other words, it can be assumed that a particular character or quality goes from one percent to 100 percent. The previous article also explains that if a gene passed on this situation, that particular trait is likely to increase in the next generation as well. The previous article could not explain how much it is and how it happens, this article may try to solve that problem. Furthermore, this article explains that these types of movements are not always helpful and can sometimes lead to other problems. This kind of explanation may be a slight deviation from the original article, however, it reaffirms that the real idea does not change for any reason. The previous article explained one more thing, which it takes more than one generation to achieve the attribute of a particular gene or trait in an individual from one percent to one hundred percent. That is, the article explains that even if a particular trait starts in one generation, it does not maximum in that generation. But this article seeks to explain another paradoxical condition within a generation.

Chance 2: Anti-clockwise movement of a gene that regulates a particular trait; *i.e.* 100% to 1%

The previous article explained that concept applies only after a particular character in an individual or a particular quality of a gene reaches its maximum quality. In other words this idea only works when a particular quality reaches one hundred percent of it. This is the first possibility of changes in a particular trait or quality of a particular gene in an individual after 100%. That is after a certain characteristic or quality reaches one hundred percent; it begins to move in the anti-clockwise direction (figure 3). This situation indicates that a particular character or quality is likely to go back to one percent after reaching 100%. That is, a return of one hundred percent to one percent. The previous article also explains that if a gene is passed on in this situation, that particular trait is likely to decrease in the next generation as well. The original article explained that this was not a good move and that it could cause a particular trait in an organism over time or the quality of the gene to decline. Furthermore, this article explains that these types of movements do not always have negative impacts and can sometimes lead to other good benefits to the individual. The previous article explained one more thing, which it takes more than one generation to achieve the attribute of a particular gene or trait in an individual from 100% to one percent. That, is the article explains that even if an anti-clockwise movement of particular trait starts in one generation, it does not reach its one percent in that generation.

Chance 3: Silent Condition

This condition is also described in the previous article under subheading Chance 3. For clarity, here is a repeat of what said in the original article. This is a condition in

which a character-controlled gene moves clockwise even when it reaches a maximum of 100%. What happens then is that the gene moves directly from 100 percent to zero percent. A figure was used in the previous article to illustrate this point, and that image has been copied to this article for completeness (figure 1). In the figure this condition mentioned as zero zone. If this happen, a particular trait is likely to disappear from a person very quickly. In the previous article, this was portrayed as an unfavorable situation for a person. This article also supports that thought, which means that if a good character disappears from a person, that person will suffer a lot. But this article explains that if a bad behavior disappears from a person in this condition, it is likely to be very beneficial for that person. That is, the outcome of such a situation will depend on the character of the situation involved.

Chance 4: “On” and “Off” Conditions

It is a condition that occurs only after the quality of the gene that controls the behavior reaches 100 percent. In this case, as described in the previous article, the gene that controls a trait has two possibilities, either moving clockwise or anti-clockwise after reaching its maximum of one hundred percent. It also suggests that the gene may take some preparation time before moving on to either of these situations. During this preparation time, the gene is likely to be “On” condition or “Off” condition. It is said that the gene is likely to be active if it is “On” condition and the gene is likely to be inactive if it is “Off” condition. The previous article states that these two conditions may occur alternately in the gene at different times, but it is not possible to say exactly when that time is.

This kind of change will affect the next generation either positively or negatively. If a gene is passed on “On” condition, the next generation will exhibit the behavior that controls that gene, according to the new concept. If a gene is passed on “Off” condition, the next generation will not exhibit the behavior that controls that gene. This may be due to the fact that the two children of a famous singer have two different qualities, one is interested in the song and the other is not at all interested in the song. According to the new concept, the gene of the child who is interested in the song may be “On” condition when transferred, but the gene of the child who is not interested in the song may be “Off” condition when transferred.

If gene transfer occurs in both of these situations, the quality of the gene will eventually decline. This is because the gene occurs after it reaches 100 percent of its maximum; subsequent changes have been described earlier in this article; that is, it is likely to include all three of the above. Such as Clockwise movement of a gene that regulates a particular trait; *i.e.* 1% to 100%, Anti-Clockwise movement of a gene that regulates a particular trait; *i.e.* 100% to 1% and also Silent condition.

In all three cases, despite being “On” condition, the anti-clockwise movement of the gene was of benefit. In the other two cases, the benefit is likely to disappear. In other words, “On” condition is possible only after the quality of the gene has reached 100%. That is if its movement is still clockwise after 100%. It becomes a “Silent”

condition and its effect disappears. If the gene moves in the anti-clockwise direction and it is “On” condition the next generation will have the quality of that gene.

Theoretical approach to the percentage of transmission of quality from one generation to the next

In this section, discussing the percentage of quality transfers from one generation to the next in the all various chances mentioned earlier. Three conceptual diagrams were used in the original article to clarify this finding. For the completion of this article, that diagrams have been copied here once again. The percentage-wise transfer of quality in different chances is explained here one by one and clearly explained.

I. Percentage difference in gene quality: Changes that occur when genes move clockwise and are transferred at that time

The details are explained in the original article, but more clarity is better for the completeness of the new concept. So that idea is explained more clearly and scientifically here. It depends on the percentage of a particular trait that controls the gene that is passed down from one generation to the next. To a particular person assume you have the ability to sing well. Also, consider that his singing level is 25% according to the new concept. Assume that the movement of the genes that control singing is also clockwise. As well as his age at that time should be considered 25.

Suppose he had a child at that age of twenty – five. That is, suppose the father is 25 years old and the child is zero years old. According to the new concept, even at age of zero, a child has 25 percent of the ability of singing because that quality was passed on directly from his parent, and the ability of the singing was 25 percent according to the new concept at the time of transfer.

In addition, the child’s singing ability will continue to increase over time until it reaches 100 percent. This is because, according to the new theory, the movement of the gene that controls this behavior is clockwise. These things are very accurately documented in the figure given here (figure 2)

One more beautiful thing can be explained very clearly from the picture. That is, at the age of 25, the father’s singing ability is 25 percent, but when the son’s age is zero (*i.e.* at birth), the child’s singing ability reaches 25 percent. Since then the two seem to be growing in parallel.

In other words, the father’s singing ability will reach 50 percent by the age of 50, but by the time his offspring reaches at the age of 25, the offspring’s singing ability will have reached 50 percent. This means that by the time the baby was born, the ability to sing had reached 25 percent. The figure incorporates variations that occur at different ages. This may be the reason why some children become very gifted in certain traits at a very young age.

II. Percentage difference in gene quality: Changes that occur when genes move anti-clockwise and are transferred at that time

These details are also explained in the original article, but more clarity is better for the completeness of the new concept. So that idea is explained more clearly and scientifically here. It also depends on the percentage of a particular trait that controls the gene passed down from one generation to the next. To a particular person assume you have the ability to sing well. Also, consider that his singing level is 25% according to the new concept. Assume that the movement of the genes that control singing is also anticlockwise. As well as his age at that time should be considered 25. Suppose he had a child at the age of twenty-five. That is, suppose the father is 25 years old and the child is zero years old. According to the new concept, even at the age of zero, a child has 25 percent of the ability of singing because that quality was passed on directly from his parent, and the ability of the singing was 25 percent according to the new concept at the time of transfer. In addition, the child's singing ability will continue to decrease over time until it reaches zero percent. This is because, according to the new theory, the movement of the gene that controls this behavior is anticlockwise. These things are very accurately documented in the figure given here (figure 3). One more beautiful thing can be explained very clearly from the figure (figure 3). That is, at the age of 25, the father's singing ability is 25 percent, but when the son's age is zero (*i.e.* at birth), the child's singing ability reaches 25 percent. After that the two seem to decrease in parallel. In other words, the father's singing ability will reach zero percent by the age of 50, but by the time his offspring also reaches the age 25, the offspring's singing ability will have reached zero percent. This means that by the time the baby was born, the ability to sing had reached 25 percent. This may be the reason why some children become very gifted in certain traits at a very young age; but after a while that particular quality may gradually decrease.

III. Percentage difference in gene quality: Changes that occur when genes are transferred at "On" condition

If the genes are passed on in the "On" condition, the quality of a particular trait will be passed down from one generation to the next. But the quality may vary according to the movement of the genes. If the genes move anticlockwise with "On" condition the quality will decrease over time, but the quality will be passed to the next generation.

IV. Changes that occur when genes are transferred at "Off" condition

According to this concept, if genes are transferred in the "Off" condition, the quality of a particular trait will not be passed from one generation to the next.

V. Changes that occur when genes are transmitted at “Silent” condition

This situation occurs when the genes move clockwise again after achieving 100% quality (figure 1). This situation is considered to be zero. This is because if the genes move clockwise after achieving 100% quality, it goes straight to zero. In this condition the genes have no quality and if the particular gene is transferred in this condition the next generation will not get the particular quality. This kind of movement of the gene can cause certain quality to disappear suddenly from a particular person. In the original article described this condition as dangerous to individuals, but it is not always dangerous to individuals. For example, if the singing quality of a famous singer suddenly disappears, it will be great loss to that particular person. But if the smoking habit disappears from a smoker, it may advantage that particular person.

Some paradoxical effect of certain behavior on certain individuals

This situation is unpredictable in a person. All other possibilities are explained in this article, and they gradually increase or decrease. But this situation is quite different from the above conditions. Some people show a particular character during his lifetime, and this particular character will quickly maximize in his life. This may be due to mutations in certain genes in his life. But his parents would not have such a habit. This character may reach the maximum level but may or may not be passed on to the next generation. Once the maximum level is reached, the particular character control gene may or may not go into “On” or “Off” conditions. If the gene is passed on in the “On” condition, the particular character may be transferred to the next generation but it may be reduced in the next generation. Similarly, if the gene is passed on in the “Off” condition, the particular trait will not be passed on to the next generation. In any case, it is reported here that paradoxical situation may be completed within a generation. This situation is not explained in the original article. Some other circumstances have been observed in connection with this paradox. Some people are very popular with some field, but their generation does not have its quality. And that generation has no quality in any area. This situation may be very dangerous for that generation. Because, human life is very difficult without even a good standard is present in a human being.

This situation may be reported in some of the most famous people in world history. This is because the quality of the particular character reaches 100% and after that they shine a lot in their field. Based on this article, when the quality reaches 100%, the character of the specific people will alternately go through the “On” and “Off” conditions. In the “On” condition, those particular people work very well. But unfortunately, in that situation they would not be interested in areas other than their particular area even in sexual life. Sometimes, they only participate in other activities on an “Off” condition subsequently the quality of the work in that situation and result also may be very poor. As result, the good qualities of that person will not be passed

on to the next generation. However, if the gene is passed on in the “On” condition, the result may change in the next generation of these individual as well.

Another reason is that, most of the genes in these individuals may be in a silent condition, but a few genes may be very active, and these genes help to perform different functions. The problem with that condition is that a few genes are very active, which means that these genes reach 100% and then they go into the “On” and “Off” conditions. In the “On” conditions of the genes, particular individual work very nicely, and if the genes are in the “Off” condition, that particular individual may not perform in a systematic way.

Also such an individual has no benefit in his “Off” condition, because in such individuals the most active genes switch to the “Off” condition and all other genes remain in the “Silent” state as described earlier. If the active genes are in the “Off” condition and the other genes are in the silent condition at the same time, the situation is very dangerous for the individual. In this situation qualities of that person will not be passed on to the next generation, if the individual participated in sex related activities. This person may alternate between “On” and “Off” states within a day according to the new concept.

Another example of the paradoxical effect

As an example, some individuals may be very bright in their student life, but these people may not perform very well in their service life/official duties or their profession. This is because all the good quality regulated genes move clockwise and it reaches 100% in the period of their student’s life. After that some genes move to the silent condition and some in the anti-clockwise direction. During their lifetime good quality may gradually diminish and they may not perform well in their service life/official duties or their profession.

Significance of the article

Evaluating a person based on current behavior may not be permanent. Because that the particular quality may change in the future. For example, if you are going to marry a famous singer, do not expect that the next generation will be interested enough in singing.

This is because his quality will reach a maximum and then quality decrease over time. At the same time, the singing quality of the next generation is also decline. But if the gene moves clockwise; the average singer may increase his singing ability over time. His next generation may have enhanced their singing ability and also it may be reached at maximum level. But must collect the information of his parents related with the singing ability. Notice that his parent has a slight interest in singing and that it gradually increases over time, and if it does increase over time, it can be assumed that the gene movement is clockwise. Based on this concept, this singing quality may maximize in the third generation.

Another example is the medical doctor; if a doctor has a little interest in this profession his second generation will be more interested in medical profession than the first generation. The third generation will be very interested in the medical profession. According to the new concept the third generation shows the highest level in his medical profession. But after achieving maximum quality, the quality may decrease over time. If so, the fourth generation may gradually lose interest in the medical profession or the fourth generation may completely lose the particular quality. But during his life time some other virtues will emerge and it will gradually increase.

Conclusion

This article tries to give more clarity than the original article. For example, the original article explains more about the positive qualities, so the article says some changes in the gene are negative for the individual. According to the original article, the clockwise movement of the gene is always positive for individuals and the anticlockwise movement of the gene is not good for individuals.

In this article, explaining that not all types of gene movements are good or bad for individuals. That is, if a good quality gene moves clockwise after reaching 100% quality it will go directly to zero. This situation is not good for individuals. However, if a bad quality gene moves clockwise after reaching 100% quality, it will go directly to zero. This situation is always good for the individuals. Because the bad quality may disappear from the person and some good qualities may be achieved.

In addition, it is reported here that there are many virtues in a person; such virtues can be good or bad. Sometimes certain qualities dominate over other qualities, and that may be due to the movement of different genes.

References

- [1] K. H. Cox, &J. S. Takahashi, Circadian clock genes and the transcriptional architecture of the clock mechanism, *Journal of Molecular Endocrinology*, **63** (2019), no. 4, R93-R102. <https://doi.org/10.1530/jme-19-0153>
- [2] M. Foo, O.E. Akman, D.G. Bates, Restoring circadian gene profiles in clock networks using synthetic feedback control, *npj Syst. Biol. Appl.*, **8** (2022). <https://doi.org/10.1038/s41540-022-00216-x>
- [3] Johanna Kraemer, Matthew Hindle, Laura K. Perby, Helle K. Mogensen, Tom H. Nielsen, Karen J. Halliday, Gerben van Ooijen, Thierry Le Bihan, and Andrew J. Millar, The Circadian Clock Gene Circuit Controls Protein and Phosphoprotein

Rhythms in Arabidopsis thaliana, *Mol. Cell. Proteomics*, **21** (2021), no. 1, 100172. <https://doi.org/10.1016/j.mcpro.2021.100172>

[4] Meltem Küçük, Umut Aksoy, Ahmet Özer Şehirli, Possible protective effects of the Bmal1 gene and melatonin on the prognosis of apical periodontitis, *Medical Hypotheses*, **162** (2022). <https://doi.org/10.1016/j.mehy.2022.110806>

[5] Németh, V., Horváth, S., Kinyó, Á., Gyulai, R., Lengyel, Z., Expression Patterns of Clock Gene mRNAs and Clock Proteins in Human Psoriatic Skin Samples, *Int. J. Mol. Sci.*, **23** (2022), 121. <https://doi.org/10.3390/ijms23010121>

[6] Rijo-Ferreira, F., Takahashi, J.S. Genomics of circadian rhythms in health and disease, *Genome Med.*, **11** (2019), 82. <https://doi.org/10.1186/s13073-019-0704-0>

[7] Santhoshkumar, R. A Concept of “Gene maturation Clock” Is it real?, *Annals of Biology*, **37** (2021), no.1, 52- 56. <http://agriop.com/a-concept-of-gene-maturation-clock-is-it-real/>

[8] Škrlec, I., Talapko, J., Džijan, S., Cesar, V.; Lazic, N.; Lepeduš, H., The Association between Circadian Clock Gene Polymorphisms and Metabolic Syndrome: A Systematic Review and Meta-Analysis, *Biology*, **11** (2022), 20. <https://doi.org/10.3390/biology11010020>

[9] Sun Han, Zhang Wenping, Wu Yongzhen, Gao Lifeng, Cui Fa, Zhao Chunhua, Guo Zhiai, Jia Jizeng (2020). The Circadian Clock Gene, TaPRR1, Is Associated With Yield-Related Traits in Wheat (*Triticum aestivum* L.), *Frontiers in Plant Science*, **11** (2020). <https://www.frontiersin.org/article/10.3389/fpls.2020.00285>

[10] Youri G. Bolsius, Matias D. Zurbruggen, Jae Kyoung Kim, Martien J. Kas, Peter Meerlo, Sara J. Aton, Robbert Havekes, The role of clock genes in sleep, stress and memory, *Biochemical Pharmacology*, **191** (2021), 114493. <https://doi.org/10.1016/j.bcp.2021.114493>

Received: August 29, 2022; Published: October 31, 2022