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Biological Cell Surveillance: Implication on Construction Cell

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Abstract
The near flawless replication of the biological cells is often attributed to the Biological Cell Cycle Control Mechanism (BCCM) to develop a complex multi-structural functional element. Central to this success is the checkpoints and the surveillance mechanism of the cell. This paper, inspired by such perfection of cellular replication investigates this mechanism to develop further insights on replication of construction cells with a special focus on the biological cell surveillance mechanism. This led to the synthesis of three concepts, namely, *process stress, process memory* and *distress signaling*. Application of these concepts has been considered as a means of overcoming the quality problems encountered in a tunnel construction project. It is argued that the application of these concepts using the RGR framework during the tunnel slab construction could have mitigated the adverse quality issues by arresting the growth of defective construction cells.

Keywords
Distress signaling, process memory, process stress, Readiness-Growth-Rest framework, surveillance

1.0 The Context
The Biological Cell Cycle Control Mechanism (BCCM) and its role in ensuring proper cell division; and its implication on construction cell has been explored to give insight on managing construction (Abeysekera & Shelke, 2015a; Abeysekera & Shelke, 2017a). This is primarily based on the identification of construction cell, which like biological cells are replicated to construct a multicellular functional structure based on the design or the DNA. However, the similarity ends here because the biological cells achieve astounding accuracy in replication of cells, while the same cannot be said for the replication of the construction cell.

How does the biological cell achieve this? Inspired by such near perfect replication of biological cells, Abeysekera & Mayur (2017) have developed a new framework using the 'simile cum metaphor' approach. Referred to as the Readiness-Growth-Rest (RGR) framework, it is to be used for the replication of a construction cell replacing the traditional plan-control or the plan-do-check-act (PDCA) models.

2.0 Aims, Objectives and Methodology
The aim of the paper is to understand further the application of the RGR framework to construction work with specific reference to the surveillance and checkpoint mechanism used by biological cells during the cell division process. In order to achieve this the following objectives have been identified, namely, the study of the above-mentioned mechanisms in biological cells, synthesizing concepts relevant for the replication of construction cells, and the application of the synthesized concepts to a real project with documented quality (and time) problems. The project chosen is a tunnel project and focusses on the construction of the arched slab segment in a tunnel project that repeats along the longitudinal tunnel axis.

Primarily, this paper adopts the case study methodology, following literature study to understand the relevance of the surveillance and checkpoint mechanism employed in the biological cell. The first author was a participant as part of the quality management team so has firsthand information on the issues at stake. The paper also draws upon the earlier established role of the BCCM in cell replication and the notion that a construction cell can be considered as a biological cell, based on the *simile cum metaphorical approach* that resulted in the development of the RGR model for construction management (Abeysekera & Mayur 2017). Accordingly, the RGR framework (Figure 1) is considered for potential enhancements based on the developed concepts.

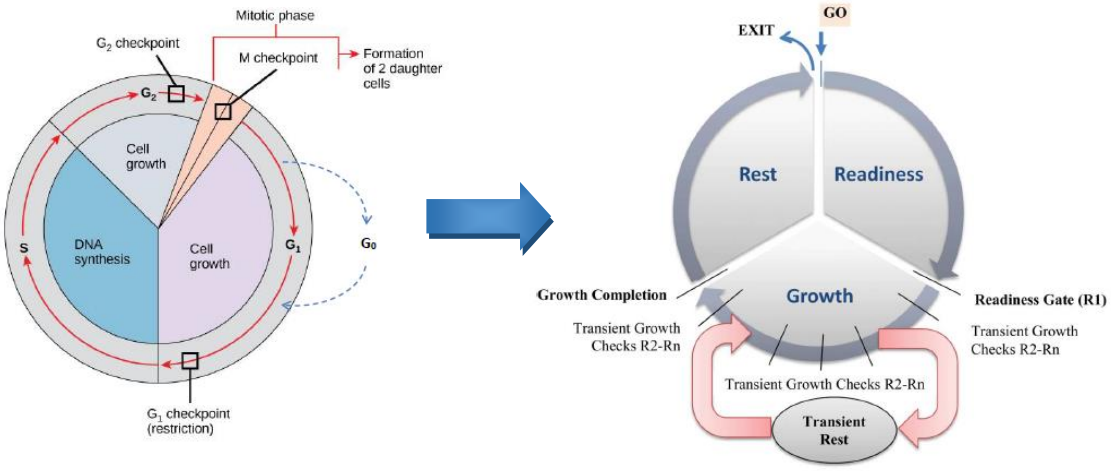

Figure 1: BCCM and RGR frameworks (Abeysekera and Mayur, 2017)

3.0 BCCM and the Readiness-Growth-Rest (RGR) frameworks

The BCCM is responsible for orchestrating the various processes of the cell cycle to achieve the sequential progression of the cell cycle (Abeyesekera andM. The cycle has two gap phases G1 and G2 between the S and M phases. In S phase, the DNA is replicated and in M phase, the cell division is completed resulting in two daughter cells having the design embedded in it for future replication. The fidelity of the cell reproduction depends on the regulatory mechanism controlled by the embedded design that ensures events of the cell cycle occur in the correct order and only after the preparations to start the next cycle is satisfactory. In other words, this readiness for cell replication is fundamental to success which is often taken lightly in construction. BCCM key features are summarized in The Table 1 given below (for more details, see Abeysekera and Mayur, 2017).

Table 1: Key features of the BCCM

Stages of Cycle	Phase of Cycle	Description
G0 (G-zero)	State of rest	Some cell may not be required to take part in replication, such cells are placed in G0 (G-Zero) state and remain in that stage until it receives signal to proceed.
G1 (Gap 1)	Interphase	Cells increase in size in Gap 1. The G1 checkpoint control mechanism ensures that everything is ready for DNA synthesis.
S (Synthesis)		Replication of DNA occurs in S-phase
G2 (Gap 2)		G2 phase-gap between synthesis (S) and mitosis (M) cell continues to grow. G2 checkpoint which will confirm the cell size, DNA replication quality and fix any identified problems before proceeding to the next phase, Mitosis for division.
M (Mitosis)	M-phase	Mitosis where the actual division of the cell will occur to yield two daughter cells. There is a checkpoint in the M stage which confirms the actual replication of the DNA is completed before the cell is split in two

As noted before, the RGR framework shown in Figure 1 is the conceptualized model for application to construction cell replication, inspired by the nearly perfect replication of cells (Abeysekera & Mayur, 2017). There are three main states viz. Readiness, Growth and Rest. The Readiness state will involve the design and development of the embedded design incorporating instructions and plans for execution of the cell-based construction. There is a gate to ensure 'Readiness' before transiting to the Growth phase to ensure satisfactory completion of Readiness state. The Growth stage is where cell construction commences at a pre-established rate and in order to ensure proper growth there are multiple Transient Growth Checks which could be driven by the standard hold points in the quality plans. The trigger for Transient arrest could be the threshold value set for parameters like the non-conformances recorded for the process in the Growth state. Such transient arrest would place the construction cell in the Rest state to address the issues before proceeding. Furthermore, the cells that are not ready for replication are also in the Rest state, until these are deemed ready for Growth. The surveillance system during the Growth state is seen as a key to ensuring the trigger for Transient rest enabling reexamination of the process, and eventually proceed further in an error free manner. The nature of the surveillance mechanism in biological cell is considered next. The developed insights based on this can be used to further refine this RGR framework.

4.0 Check Point and Surveillance Mechanism in Biological Cell

This section considers the working of the checkpoints and the significance of the surveillance mechanism in a biological cell. What is the surveillance mechanism used and what is the trigger for the checkpoint activation, and hence effective control over the cell division process? Organism are said to be communities of cooperating cell, and the corporation includes strict control on when cells divide to create a new cell. The consequences of breakdown in the controls in even a small number can be seen in cancer, a disease of uncontrolled cell division (eventually killing the organism) (Cassimeris et al. 2011, p. 674). This highlights the importance of the accurate operations of the surveillance mechanism and the checkpoints, given the disastrous consequences of lack of cellular control on cell proliferation.

4.1 Check Points Mechanism

The level of concentration of proteins within the cell are the basis of operation of the checkpoints. For example, the entry of cell into M phase is triggered by activation of protein kinase called as MPF (Maturation Promoting Factor). The MPF comprises two units namely the Catalytic Subunit, also known as cyclin dependent kinase [Cdk] and Regulatory Subunit. The Regulatory Subunit is the family of proteins called as cyclins (Karp, 2007). The activity of the Catalytic Subunit is dependent on the concentration of the cyclins. When the cyclins concentration is low the kinase [Cdk] is inactive and when the concentration is at the sufficient levels, the kinase [Cdk] is activated. Such transient activation allows the passage through the checkpoints. The concentration of cyclins rise and fall during cell cycle as a result of changes in the rate of synthesis and destruction of protein molecules. In mammalian cells at least 8 different cyclins and half a dozen different Cdks play role in cell cycle regulation. The passage through the checkpoints require the transient activation of Cdk by specific cyclins, as the cell passes through stages from one cell division to next. Thus, the Catalytic Subunit, appropriately also known as Cdk is activated or inactivated based on the concentration of specific cyclins, enabling the control of the checkpoints. Clearly, the checkpoints are controlled by the signals monitoring the concentration levels.

4.2 Surveillance Mechanism

Many signals registered at checkpoints come from cellular surveillance mechanisms inside the cell. These signals report whether crucial cellular processes that should have occurred by that point have in fact been completed correctly and thus whether or not the cell cycle should proceed. The checkpoints also register signals from outside the cell (Reece et al., 2011, p. 243). Three major check points in the various stages of cell cycle are identified in Figure 1 above. The surveillance mechanism in the Mitosis (M-Phase) where the actual division of the cell will occur to yield two daughter cells is considered which confirms the actual replication of the DNA is completed before the cell is split in two. This transmission of the DNA or the blueprint to the daughter cells is of utmost importance as this contains the codes for the very survival

and accurate **replication** of the cell. According to Lambrus and Holland (2017), the cells have evolved certain precautions to preserve their DNA content during mitosis and avoid potentially oncogenic errors (leading to tumors). This is the cell proliferation outside of the cellular control mechanism, which is considered abnormal (Lax & Thomas, 2002) and can have disastrous consequences for the survival of the organism (Lax & Thomas, 2002; Martin, M, Ross, Jones, & Henderson, 1990; Simon, 1996).

Additionally to the checkpoints, recent observations have identified mitotic failsafe referred to as the mitotic surveillance pathway. This pathway triggers a cell cycle arrest to block the growth of potentially unfit daughter cells. This is activated by both prolonged mitosis and centrosome loss (Lambrus & Holland, 2017). This effectively curbs the growth of cells that do not have proper replication of the DNA. How such sensor conduct surveillance and activate the corrective action is considered next.

Based on data collected, Lambrus and Holland (2017) have determined that the gene responsible for DNA damage signaling, also plays an independent role to monitor the centrosome. The centrosome in the animal cell contains material that functions throughout the cell cycle to organize the cell's microtubules, (Reece et al., 2011, p. 235). The centrosome duplicates during G2 of Interphase and forms the mitotic spindle with the microtubules extending from it. This mechanism allows for the separation of the duplicated DNA (two sister chromatids) at each of the ends and facilitates the two liberated daughter chromosomes to form in the cell with each having equivalent and complete collections of chromosomes, marking the completion of mitosis.

The study by Lambrus and Holland (2017) points to at least three genes having indirect role in monitoring centrosome number. The loss in centrosome, as well as too much production of centrosome leads to cell cycle arrest. Such monitoring by multiple genes point to the redundancy built in this mechanism, which according to Stelling, Sauer, Szallasi, Doyle, and Doyle (2004) is the simplest strategy to protect against failure of specific component by providing for alternative ways to carry out the function that the component performs. Lambrus have deduced based on further findings loss in centrosome and too much production is indirectly detected through 'symptoms' associated with either loss or gain of centrosome. This is referred to as symptoms-based surveillance, described in next section.

4.3 Symptoms-based Surveillance

The idea of mitotic clock is introduced wherein the key defect observed in cells lacking centrosomes is that they are slower to assemble spindles and thus spend longer time in mitosis. An earlier pioneering study has demonstrated that prolonged mitosis surpassing a threshold duration is sufficient to trigger a cell cycle arrest in daughter cells despite the completion of an otherwise normal division. Lambrus and Holland (2017) have confirmed that the genes for centrosome surveillance also are responsible for mitotic timer functionality, thus there is possibility that centrosome loss triggers a cell cycle arrest by causing mitotic delay.

This is significant, because the surveillance has now introduced the element of time as a parameter. The completion time established for process is now monitored. Interestingly, one such delay in mitosis does not necessarily cause cell cycle arrest, however two such prolonged divisions will ensure cell cycle arrest. Lambrus and Holland (2017) propose that cell integrate '*mitotic stress'* over several divisions and also refer to '*memory model'* wherein the granddaughter cells can *'recall'* the stress from prolonged mitosis more than one full cell cycle earlier, and induce cell cycle arrest. This appears similar to the one of threshold parameters like non-conformance report (NCR) for inducing transient arrest of construction cell (Abeysekera & Shelke, 2017b). This threshold parameter of NCR has been further referred to in the conceptualized RGR framework to induce a transient cell cycle arrest to fix the process before proceeding further with construction (Abeysekera & Mayur, 2017).

The insights gained from the cell surveillance mechanism is used to synthesize concepts which can be applicable to the replication of the construction cell. This is considered next.

5. Synthesized Concepts

Three concepts have been synthesized for application to construction cell based on the surveillance mechanism employed in the cell. The cell appears to use process timer for surveillance and integrates the 'process stress' observed over the cell cycle activities and memorizes such occurrences before issuing signal to induce cell cycle arrest. The synthesized concepts are: (a) Process stress (b) Process memory and (c) Distress signaling to ensure 'process stop' based on symptoms

These concepts, while developed based on the growth of the mitotic phase, can be considered for the G-growth phase in the RGR framework (Figure 1). This phase is the actual construction phase, following the R or readiness phase. This is the phase of RGR framework, which can best utilize the concepts to monitor the construction process for stress and issue distress signals to induce transient state of rest.

The built in process timer is important for construction and activities which are delayed needs to investigated closely to determine the cause of such delays. While project schedule may resemble the timer or built-in clock, the efficacy of such timer or schedule is in question. Koskela and Howell (2008) have considered the adherence to a complete, priori statement of intent as illogical and instead advocated strategies that remain flexible and adaptive. Thus, the activities identified in the 2 week or 3 week look ahead offers more reliable 'feel' of ground situation and there needs to be analysis as to why the activities identified in the 2 week or 3 week look ahead plan has not been completed. Likely, any such identified delay is an indication of defects - in terms of interface issues, availability of men and material at the right place and right time, technical or process issues with the methodology etc. Any undue delay in achieving the completions of activities is an indication of process stress, which needs to activate the transient stop to the process. Review of plan and activities needs to be considered before proceeding further. This is well in line with the RGR model proposed by Abeysekera and Mayur (2017), wherein a transient state of rest is required for the process once triggered.

The integration of the process stress is a deliberate observation and record of process output not in line with the desired outcomes. For example, if there is a time limit based for an activity or productivity numbers like average concrete pour volume achieved, a record of such process values is maintained to determine the variation from the benchmarked values. This is what can be referred to as process memory, but memory alone is insufficient to ensure quality. While a singular deviation of time limit cannot form the basis to trigger quality alarm, such reoccurring events for the activity is likely to be symptomatic of potential quality issues. The time, especially for repetitive activities is likely to decrease given the effect of the learning curve, thus multiple record of variation of the process time may be indicative of process stress. This, in effect is variation of process parameter, measured in terms of time consumed for the activity which the system 'memorizes' for later use which in turn serves as the basis for initiating distress signal which may throw a process into a temporary state of rest. A case study is considered for application of such concepts.

6. Case Study Analysis-Slab Construction in Tunnel

The case of construction of tunnel slab in a large infrastructure project is considered. The first author was a participant in this case in the role of quality management. The Figure 2 below is depicting the process of concrete pour of $3200 m^3$ for slab construction in a tunnel.

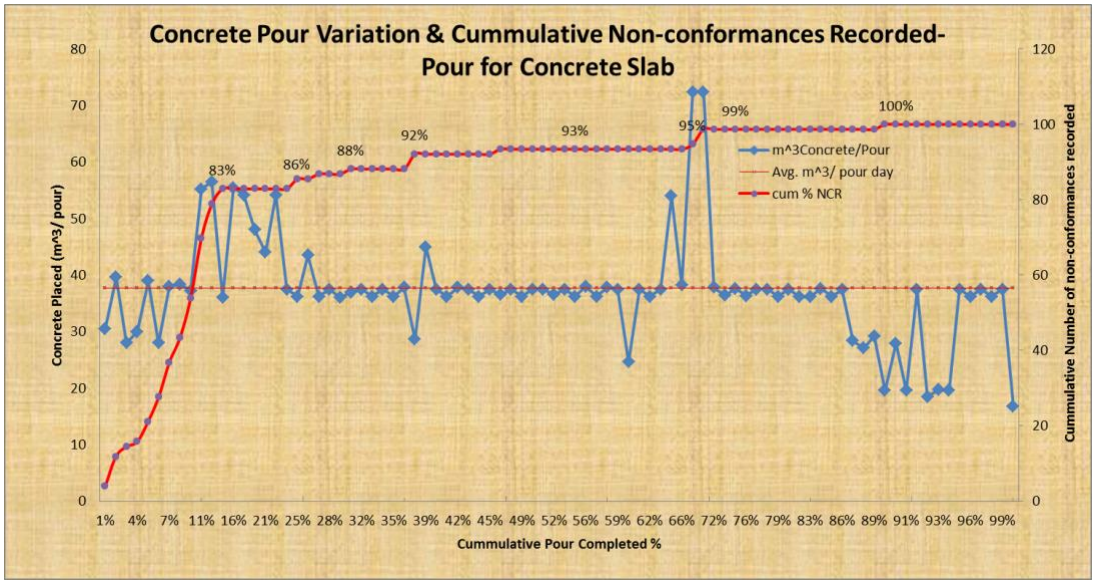

Figure 2: Plot of process for concrete pour volume and quality issues for tunnel slab construction

As evident, most of the quality issues ar recorded where the variation of the process is observed. The table 2 below depicts the occurrences of quality issues over the complete process.

Table 2: Process progression and quality issues

% Completion of job	Number of concrete pours	Number of Quality Issues or Non conformance	% QA Issues
First 25% of total concrete poured	19	65	86%
Between 26% and 50% of total concrete poured	22	6	8%
Between 51% and 74% of total concrete poured	19	4	5%
Final 26% of total concrete pour	26	1	1%
Total (3200 m^3 concrete)	86	76	100%

6.1 Analysis-Based on Surveillance Mechanism Concepts

An earlier case study of concrete pour variation for tunnel slab construction has shown remarkable co-relation with respect to quality issues recorded when the process variation in terms of average concrete pour volume varied from the average for the overall concrete pour process. Nearly 85% of quality issues were observed within the first 25% of the concrete pour (Abeysekera & Shelke, 2013; Abeysekera & Mayur, 2017). Could it be the lack of process stress integration and distress signaling for process stop contributing to this?

The process of concrete pour has progressed despite the quality issues, which were duly recorded. It seems in absence of process to consider such variations as 'process stress' the significance of the data in hand was not realized. There is also absence of distress signal mechanism to halt the process. The schedule for this activity can be considered as a timer because it has the duration, however, the actual record of the time required to complete the pour and related activity can be deemed as the record of the process stress. This is obvious, because a program schedule does not consider any quality related issues in it, neither in most cases it has provision for quality checks, while the actual record of time for the acivity has integrated the processs stress.

Positing that the record of the process time (time for concrete pour) could be the record of the process stress based on the time either exceeding or falling short of the average, then provides powerful tool of surveillance, wherein the process is not halted based on singular variation. Akin to the symptoms-surveillance employed by the cell, this can be a reliabel indicator to issue a process distress signal to induce a transient state of rest, giving an opportunity to re-set or evalute the factors causing such variation.

In this tunnel case, in hindsight it is clear that the progressive record of such ciritial process had signals embedded within it. This could be one of the major 'symptoms' to monitor. The identifcation of critical process and its record (is usallly avaialble) on most project but hardly analysed for such trigger given the lack of knowledge of the value such record holds. This is where the concept of process memory to analyse, compare and recall the construction cycle time to indicate likely issuance of a distress singal can abe useful.The surveillance mechanisms for symptoms in this case, the time taken for the process and the likelihood that such record also captures the process stress by capturing the variation, is highlighted by this developed concepts based on celluar surveillance mechanism. It is likely, triggering a transient state of rest then, as indicaed by the RGR framework to reset the process would have led to lesser quality issues encountered, post process reset.

The use of distress signal based on such anlaysis of process records to induce transient state of rest provides a new avenue to nudge the construction industry to consider the early signs for likely emerging quality issues with the process. A benchmark needs to be set for such distress signals, wherein a particular value is considered as a trigger to reexamine the process. In the RGR model, Abeysekera and Mayur (2017) have identifed the non-conformances recorded for setting the threshold to induce transient state of rest, this study has now indicated the process stress as an important indicator for setting the transient construction cell cycle arrest. Had the tunnel project, the awareness of such signals, and especially the distress signal to induce transient state of rest to review and reset the process, it is likely the number of quality issues would have been lesser. While there was surveillance, inspections carried out during the slab construction, the question is was this effective? Did it cause timely process review? From the Figure 2, it is clear that for the first 25% of the pour there was an increasing trend in quality issues. Likely, with evidience of process stress analysed in real time would have induced process review early to achieve stabilization.

The signals in a biological cell, issued, after it seems due diligence given the redundancy built into this mechanism are hard to ignore. The tunnel construction has lacked such distress signalling system for quality issues, which would have induced transient state of rest to address the process issues. Traditional tools like NCR induce a process hold, however this is post quality event. These synthesized concepts highlight the significance of the process records, process memory to decode the embedded signals and generate distress signalling. These would have provided an opportunity during the tunnel construction to evaluate the process, likely assisting in reducing quality issues, and thus achieve improvement in quality.

7. Conclusion and Recommendations

In most large projects, there seems to be progress records which are actually recording the time for activity completion. Creative use of such seemingly routine records with the identified quality issues and superimposing such data could provide a powerful surveillance tool. Such record over time, can be considered as the capture of the process stress and thus an indicator of the likely quality issues. The current quality practices in construction are well designed to keep record of quality events and recording the corrective actions taken, i.e. its strength appears in managing a quality event, rather than preventing quality event from happening, let alone signalling the likelihood of emerging quality issues. The project can use this as a tool as an early indicator of quality issues and be prepared to avoid quality issues, rather than marshal resources to fix the issues once they have occurred. There exists mechanism to 'hold' the process in the current quality management practice to inspect critical parameters before proceeding, however does it have the potency of the cellular signalling to stop the process? That such hold points or

witness points for the process as prescribed in the quality plan are altogether missed is a likely event. This is where cellular distress signalling can be considered to ensure transient process stops, before quality event has occurred to re-examine the process before proceeding. The checkpoints in biological cells are unforgiving and a stop means 'stop'. This is one of the factors ensuring nearly perfect replication. In construction industry, it is an opportune time to consider the significance of signals to induce process stops at checkpoints to ensure there is reduction in quality issues.

The tunnel slab construction would have benefitted in hindsight, from application of above mentioned concepts. While credit needs to be given to the existing quality system to record quality events for such analysis, it is recommended that application of such developed concepts and the RGR framework for construction cell replication, Attempting to fix the quality issues appears to be a current trend, while cellular constuction allows for signalling likley quality events before occurrence.The RGR framework needs to be upated with the new trigger point like process stress. While threshold for the non-conformances is one of the trigger point, the process stress is likely to enhance the RGR framework to be more responsive to the construciton cycle replication in terms of monitoring for process stress and issuing distress signals. For long, the construction industry has carried on with activities to meet the program schedule, more often spending more time and money to fix the resulting defects. This is where the distress signaling based on process surveillance and output can be used to induce transient cell cycle arrest to reset the process however, the failsafe working of the checkpoints of biological cell based on surveillance signals, needs to be considered for adaptation in the construction industry. Further work here entails refinement of the RGR framework and development of robust methodology to ensure the relevance of such model to replication of construction cells, and thus by extension to construction industry.

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