

Supplementary File for BioBlock: A Blockchain Analogous Mechanism for Integrity in IoBNT-based Drug Delivery Systems

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I. PROOF OF LEMMA 1

Lemma 1. *Considering a single target T_i , the expected number of bionodes $\mathbb{E}(\eta)$ that detect the target is formulated as follows:*

$$\mathbb{E}(\eta) = \left[\frac{e^{-\varrho\pi r_n^2 x} - e^{-\varrho\pi r_n^2}}{1 - e^{-\varrho\pi r_n^2}} \right] \sum_{i=1}^{\infty} \eta_i \quad (1)$$

Proof. In this scenario, we consider that there is a single target T_i with traceable radius, r_i . The area Λ of the target T_i getting detected by x number of bionodes in its circumference is given by $\Lambda(x) = \pi r_n^2 x$. We consider that the number of bionodes follow a Poisson distribution.

$$P(|\alpha| = \gamma) = \frac{(\varrho\Lambda)^\gamma \exp(-\varrho\Lambda)}{\gamma!} \quad (2)$$

where ϱ denotes the bionode density given by $\frac{\alpha}{\mathcal{A}}$. The probability that the target, T_i is not detected for the number of bionodes $\eta \geq x$ is computed from the probability that there is no bionode in the circumference of the target, which is computed as follows:

$$P(\eta \geq x) = P(|\alpha| = 0) = \exp(-\varrho\Lambda) \quad (3)$$

The expected number of bionodes covering the target is computed as follows:

$$\begin{aligned} \mathbb{E}(\eta) &= \sum_{i=1}^{\infty} \eta_i P_i(\eta \geq x) = \sum_{i=1}^{\infty} \eta_i [1 - P_i(\eta < x)] \\ &= \left[\frac{e^{-\varrho\pi r_n^2 x} - e^{-\varrho\pi r_n^2}}{1 - e^{-\varrho\pi r_n^2}} \right] \sum_{i=1}^{\infty} \eta_i \end{aligned} \quad (4)$$

where ∞ is the maximum number of bionodes considered in the nanonetwork. When x is very small, $e^{-\varrho\pi r_n^2 x} \approx 1$, so that the term arising from the probability factor reduces to 1. Consequently, the expected value depends on the random variable, η .

$$\mathbb{E}(\eta) \approx \sum_{i=1}^{\infty} \eta_i \quad (5)$$

Now, η being a non-negative random variable the series does not converge and is determined by the value of ∞ . When ∞ is very large, the expected number of bionodes increases to take an infinite value. However, when ∞ takes a countable value

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the series converges to a finite value. Thus it can be inferred that a mobile target will be detected by at least η bionodes, all having equal communicating range. \square

II. PROOF OF LEMMA 2

Lemma 2. *Let ϑ be the number of vesicles enclosing information molecules contained in a bionode transmitted to the target T_i and p is the probability of each vesicle reaching the target successfully. Then the probability of successful information delivery \mathcal{B} of the entire system follows a Gaussian distribution formulated as follows:*

$$P(\mathcal{B}_n) = f(\mathcal{B}) = \sqrt{\frac{n}{2\pi p(1-p)\vartheta}} e^{-\frac{n(\beta-p\vartheta)^2}{2p(1-p)\vartheta}} \quad (6)$$

Proof. Once a target is detected by n number of bionodes, each of them transmit the contained vesicles independently. The outcome of these independent transmissions is characterized by either a success or a failure. Based on this scenario, the event is equivalent to the Binomial distribution. The probability that ψ vesicles are successfully delivered to the target out of ϑ vesicles is given as follows:

$$P(\beta = \psi) = \binom{\vartheta}{\psi} \cdot p^\psi (1-p)^{\vartheta-\psi} \quad (7)$$

where p is the probability of success with which each vesicle reach the target and β is the random variable which denotes the number of vesicles that reaches the target from one bionode n_i . Thus the probability of successfully receiving Ψ vesicles by the target from n bionodes is given as follows:

$$P(\mathcal{B} = \Psi) = \prod_{i=1}^n \left(P(\beta_i = \psi) \right) \quad (8)$$

For n independent bionodes, the expected number of vesicles that reaches the target is computed as follows:

$$\mathbb{E}(\mathcal{B}_n) = \sum_{i=1}^n \mathbb{E}(\beta_i) = np\vartheta \quad (9)$$

Since $n \rightarrow \infty$, $\mathbb{E}(\mathcal{B}_n)$ diverges to take ∞ value. Thus to limit the overall distribution of \mathcal{B}_n , we apply *Central Limit Theorem*. The corresponding mean and variance for \mathcal{B}_n is given as follows:

$$\mathbb{E}(\mathcal{B}_n) = np\vartheta, \quad \text{Var}(\mathcal{B}_n) = \frac{p(1-p)\vartheta}{n} \quad (10)$$

Thus the probability $P(\mathcal{B}_n)$ converges to a Gaussian function obtained as follows:

$$f(\mathcal{B}) = \sqrt{\frac{n}{2\pi p(1-p)\vartheta}} e^{-\frac{n(\beta-p\vartheta)^2}{2p(1-p)\vartheta}} \quad (11)$$

\square

III. PROOF OF LEMMA 3

Lemma 3. *Considering a nanonetwork at any time interval Δt , the total energy utilized \mathcal{E}_t in successful drug delivery is obtained as follows:*

$$\mathcal{E}_t = \frac{KTR^2}{2t_p D} + \kappa\mathcal{E}_r + \mathcal{E}_v + \kappa_a\mathcal{E}_a \quad (12)$$

Proof. We consider an area of $a \times b$ with n uniformly distributed bionodes. Each bionode has a different number of neighboring bionodes in its communication range with radius r_n . In order to relay information in the nanonetwork, the bionode propagates in its neighborhood until the protein sequence matches. The random walk of the bionodes in a confined area can be defined by the transition matrix $T = [T_{ij}]$, where T_{ij} refers to the probability of bionode b_i to go to bionode b_j . We define the time a bionode takes to reach another bionode with matched sequence as the passage time. Thus the passage time refers to the number of steps a bionode takes for its random walk to be stationary. The second largest eigenvalue of the transition matrix T determines the asymptotic rate of convergence of the random walk. Considering that the second largest eigenvalue is close to 1, the passage time t_p is obtained as follows:

$$t_p = \frac{1}{1 - e} \quad (13)$$

where $1 - e$ is the rate of convergence of the random walk. Once a bionode b_j with matched sequence is detected, the bionode b_i ensures successful information relaying. Thus a bionode utilizes energy in propagation, releasing plasmids, transferring vesicle containing information molecules, and finally authenticating BioBlock. The energy consumed in propagation \mathcal{E}_p can be computed from the distance covered by a bionode along the random walk until it becomes stationary. Thus we compute the mean distance between any two bionodes is computed as follows:

$$\mathbb{E}(d^2) = \int_{\theta=0}^{2\pi} \int_{r_n=0}^R r_n^2 \rho(r_n, \theta) r_n dr_n d\theta = \frac{R^2}{2} \quad (14)$$

where the joint probability density function ρ of the random variables r_n and θ is represented as $\rho(r_n, \theta) = \frac{1}{\pi R^2}$. The energy utilized in releasing plasmids is based on the number of produced plasmids κ , which involves $\kappa \times \mathcal{E}_r$ of energy. We consider that after conjugation, the bionode b_i passes one vesicle loaded with drug molecules to the bionode b_j . The energy involved in transferring the vesicle containing information molecules is represented as \mathcal{E}_v . To authenticate the BioBlock information, the energy cost involved depends on the number of generated blocks (adhered plasmids) κ_a , which is given by $\kappa_a \times \mathcal{E}_a$. Thus at any time interval Δt , the total energy utilized is obtained as follows:

$$\begin{aligned} \mathcal{E}_t &= \mathcal{E}_p + \kappa\mathcal{E}_r + \mathcal{E}_v + \kappa_a\mathcal{E}_a \\ &= \frac{KTR^2}{2t_p D} + \kappa\mathcal{E}_r + \mathcal{E}_v + \kappa_a\mathcal{E}_a \end{aligned} \quad (15)$$

where K is Boltzmann's constant, T is absolute temperature, and D denotes the diffusion coefficient. \square