Impacts of SW-ARQ on the Latency and Reliability of Diffusive, In-sequence Molecular Communication

Kento Furuhashi*§, Junichi Suzuki*, Jonathan S. Mitzman*, Tadashi Nakano‡, Yutaka Okaie‡ and Hiroaki Fukuda§
*University of Massachusetts, Boston, Department of Computer Science, Boston, MA 02125, USA
‡Osaka University, Graduate School of Frontier Biosciences and Institute for Academic Initiatives, Osaka 565-0871, Japan
§Shibaura Institute of Technology, Department of Information Science and Engineering, Tokyo 135-8548, Japan
Email: {kento, jxs}@cs.umb.edu, {tadasi.nakano, yokaie}@fbs.osaka-u.ac.jp, hiroaki@shibaura-it.ac.jp

***Abstract*—This paper studies a feedback-based communication protocol for bio-nanomachines to reliably transmit and receive a series of molecular messages through diffusive transports in a particular order. Based on the Stop-and-Wait Automatic Repeat Request (SW-ARQ) mechanism, the proposed protocol leverages redundant molecule transmissions, molecule delivery acknowledgement and timeout-based retransmissions to enhance the latency and reliability of in-sequence molecular communication. Simulation results demonstrate that the protocol substantially improves latency, jitter and transmission failure rate. They also illustrate how environmental and protocol parameters impact those communication performance metrics.**

I. Introduction

Diffusive molecule propagation is known inherently unreliable, and therefore it causes extremely long latency, large jitter, high molecule loss rate and low capacity in molecular communication [1–3]. This paper addresses the reliability issue in diffusive, aqueous molecular transports and studies a communication protocol for bio-nanomachines to reliably transmit and receive a series of *information molecules*, which encode and carry information by means of molecules, in a particular order.

Reliable in-sequence molecule delivery can play critical roles in various biomedical and healthcare applications. For artificial morphogenesis applications in regenerative medicine, bio-nanomachines made of living cells are designed to divide and grow to form three-dimensional multi-cellular structures such as tissues and organs. Molecular communication allows those bio-nanomachines to communicate with each other using *artificial morphogens*, which are modeled as the information molecules that encode morphological information. Reliable in-sequence molecule delivery is a critical foundation to reliably control communication patterns (e.g., the order of propagated artificial morphogens and the interval of artificial morphogen propagation) for adjusting the growth and differentiation of bio-nanomachines.

In order to facilitate reliable in-sequence molecular communication, the proposed protocol employs Stop-and-Wait Automatic Repeat Request (SW-ARQ) [4], which is feasible enough to realize with simple computation and memory functions in bio-nanomachines. It performs *bi-directional* interactions between a transmitter (Tx) bio-nanomachine and a receiver (Rx) bio-nanomachine. The Tx bio-nanomachine duplicates an information molecule and transmits them to the Rx bio-nanomachine. Upon receiving one of them, the Rx transmits duplicated acknowledgement (ACK) molecules to the Tx. The arrival of an ACK molecule at the Tx indicates that the Rx has received an information molecule that is associated with the ACK molecule. This ACK arrival triggers the Tx to transmit the next information molecule(s). If the Tx never receive ACK molecules within a timeout period, it re-transmits duplicated information molecules to the Rx.

This paper evaluates the proposed protocol through simulations that are configured with biologically-feasible parameters. The simulation study analyzes how the proposed protocol impacts communication performance, namely latency, jitter and failure rate, in comparison to traditionally major molecule transmission schemes such as single-molecule transmission and duplication-based transmission. Compared to a duplication-based transmission scheme, which does not involve ACK-based retransmissions, the proposed protocol gains 1.28x speedup in latency, reduces latency jitter by 38.7% and reduced transmission failure rate by 70%. Simulation results also reveal how environmental parameters (e.g., Tx-to-Rx distance) and protocol parameters (e.g., retransmission timeout period) impact communication performance and other characteristics such as energy consumption.

II. Related Work

Nakano et al. [5] and Felicetti et al. [6] study feedback-based rate control schemes for molecule propagation in diffusive transports. Those schemes are designed to ensure delivering a given number of information molecules to the Rx while preventing the Tx from transmitting the molecules faster than the Rx reacts. While in-sequence delivery of information molecules is out of the scope in [5, 6], this paper focuses on an in-sequence and at-least-once delivery semantics.

In-sequence molecular transmission is studied with SW-ARQ schemes for diffusive transport in [7] and bacterial communication in [8]. This paper is similar to [7, 8] in that the two papers utilize SW-ARQ. However, unlike [7, 8], this paper examines SW-ARQ in collisional environments where molecules collide with each other. This paper extends [9] by reporting an extended set of simulation results that are obtained with more reasonable simulation configurations.

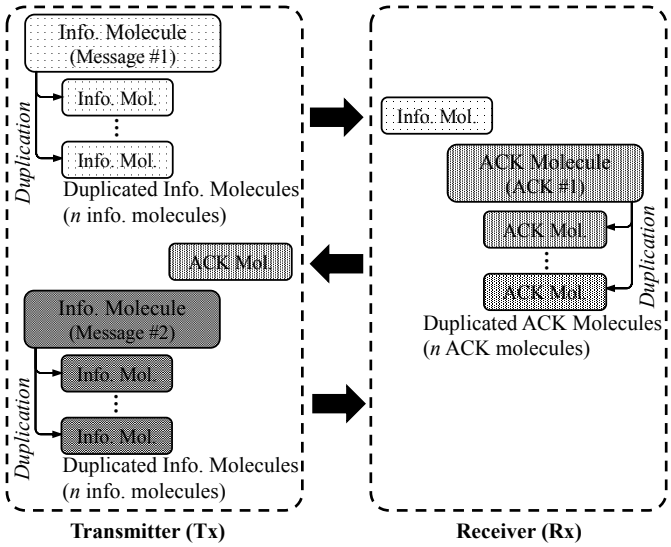

Fig. 1. Interactions between the Tx and the Rx

III. The Proposed SW-ARQ Protocol

This paper assumes a bounded, cubic environment in which the Tx and Rx bio-nanomachines are placed to perform the proposed SW-ARQ protocol for molecule transmission.

The proposed protocol allows the Tx to propagate n duplicated copies of an information molecule that encodes a particular message (Fig. 1). Once the Rx receives at least one of those information molecules, it propagates n duplicated ACK molecules, each of which indicates a receipt of the message. The Rx is assumed to capture an information molecule when the molecule arrives at the surface of the Rx. Upon receiving at least one of the ACK molecules, the Tx propagates n information molecules that encode the next message (e.g., Message 2 in Fig. 1). The Tx is assumed to capture an ACK molecule when the molecule arrives at the surface of the Tx. Note that the Tx stops transmitting subsequent messages until the Rx acknowledges all prior message transmissions.

If the Tx does not receive an ACK molecule for a message in a certain timeout interval, called retransmission timeout interval (RTO), it retransmits another set of n information molecules for the message. Molecule retransmission may occur multiple times until the Tx successfully receives an ACK molecule or exceeds a predefined number of retransmissions.

If the Rx does not receive any information molecules that encode the i-th message within RTO after sending ACK molecules for the $(i-1)$-th message, it retransmits another set of n ACK molecules for the $(i-1)$-th message.

The proposed protocol is applied to diffusive transports where both information and ACK molecules diffuse through the environment via random thermal motion. Diffusive movement is governed by the diffusion coefficient D on each dimension: $D = \partial x^2/(2 \times \partial t)$. x denotes the distance of molecular movement during an amount of time t. When a molecule collides with another molecule, it randomly moves to another position with D.

IV. Simulation Evaluation

This section evaluates the proposed SW-ARQ protocol through simulations based on the MolComKit simulator[1]. Table I shows simulation parameter settings, which follow experimental findings in biomedical engineering (e.g., [11, 12]). Every result is shown based on 1,000 independent Monte-Carlo simulations (particle-based simulations).

TABLE I
Parameter Settings

Parameter	Value
Tx to Rx distance (d)	30, 50, 70 or 90 μm
Size of the environment	$4d$ μm $\times$ $4d$ μm $\times$ $4d$ μm
Diameter of Tx and Rx	5 μm
Diameter of an info/ACK molecule	1 μm
Diffusion coefficient (D)	0.5
Length of a nucleobase	0.34 nm
# of nucleobase pairs in a molecule (p)	52,000
Max # of message retransmissions	5
# of duplicated info/ACK molecules (n)	1, 10, 20, 30, 50 or 100

The size of the environment varies according to the distance between the Tx and Rx (d). The boundaries of the environment are simulated in a non-replusive manner. Molecules do not rebound against boundaries. Molecule-to-molecule collisions are also simulated in a non-replusive manner. Each molecule is prohibited to move to the location of another molecule. Colliding molecules do not rebound with each other.

The diameter and diffusion coefficient (D) of a molecule is determined based on the experimental results in [12]. When $D = 0.5$, each molecule is 17.6 nanometers long and it contains 52,000 pairs of nucleobases. It can encode 13,000 bytes of data. All simulations are carried out to perform a single message transmission, in which duplicated information molecules travel from Tx to Rx and duplicated acknowledgement (ACK) molecules travel from Rx to Tx.

Figs 2 and 3 show the cumulative probability distribution of roundtrip time (RTT) between Tx and Rx, which are located 30 and 90 μm apart, respectively. The number of duplicated molecules per information/acknowledgement (n) varies from 1 to 100. For example, SW-ARQ-20 means that the Tx sends out 20 redundant information molecules for a message and the Rx sends out 30 redundant ACK molecules for an acknowledgement. RTT sums up the time that one of redundant information molecules first hits the Rx and the time that one of redundant ACK molecules first hits the Tx. Molecule retransmissions never occur (RTO=∞). Fig 4 shows the median RTT under different Tx-Rx distances (d). Figs. 2 to 4 demonstrate that RTT increases as Tx-Rx distance (d) grows. RTT improves significantly as the redundancy in molecule propagation (n) increases. Fig. 4 illustrates that, when info/ACK molecules are never duplicated (n=1), the median RTT increases from 237,193 to 6,520,084 seconds (65.8 hours to 75.4 days) as Tx-Rx distance (d) increases from 30 to 90 μm. When $n = 20$, the median RTT increases from 5,322 to 263,186 seconds (1.4 hours to 73.1 hours) as d increases from 30 to 90 μm.

[1] http://www.cs.umb.edu/~jxs/molcomkit/

Figs 5 and 6 show how the median RTT and RTT jitter change as the redundancy in molecule propagation (n) varies. The jitter of RTT is measured as the standard deviation of RTT results. Both the median RTT and RTT jitter greatly improve as n increases. Note that RTT jitter stays very high regardless of n; it is similar to, or even higher than, the median RTT. For example, when $n = 20$ and $d = 90$ μm, the median RTT is 263,186 seconds (73.1 hours) and RTT jitter is 280,603 seconds (77.9 hours).

Fig. 7 illustrates how the rate of message transmission failure changes as the redundancy in molecule propagation (n) varies. A message transmission is considered failed if RTT exceeds the median RTT. As shown in Fig. 7, the failure rate decreases as n increases. When $d = 30$ μm, the failure rate reaches zero with $n = 100$. However, when $d = 90$ μm, the failure rate stays higher than 50% even with $n = 100$.

For the subsequent simulations, the redundancy in molecule propagation (n) is set to 20. This parameter setting is well-balanced with respect to communication performance (median RTT and RTT jitter), communication reliability (message transmission failure rate) and energy consumption. When $n = 20$, communication performance is significantly preferable compared to the case with $n = 1$ and close enough to the cases with $n > 20$ (Figs. 5 and 6). When $n = 20$, the average number of molecule-to-molecule collisions in a simulation is sufficiently low (Fig. 8). However, when $n > 20$, the number of collisions exponentially increases, which implies significantly higher risks to increase RTT jitter. Higher redundancy in molecule propagation (n) requires higher (chemical) energy consumption for Tx and Rx to duplicate molecules. Fig. 9 shows how much energy Tx and Rx spend for a message transmission with n information molecules and n acknowledgment molecules. Energy consumption is computed as $\Delta G^\circ \times p \times 2n$. ΔG° is 45.6 kJ/mol where $mol = 6.022 \times 10^{-23}$. p denotes the number of nucleobase pairs in a molecule (Table I).

Molecule retransmission is enabled (RTO$\neq\infty$) in the subsequent simulations. The maximum number of retransmissions for each information/acknowledgement is set to 5 (Table I). The following four schemes are examined to configure retransmission timeout (RTO):

- RTO-1: $2 \times RTT_{med}$
- RTO-2: $RTT_{med} + \frac{1}{3} \times RTT_{std}$
- RTO-3: $RTT_{med} + \frac{1}{2} \times RTT_{std}$
- RTO-4: $RTT_{med} + RTT_{std}$

RTT_{med} and RTT_{std} denote the median RTT and the standard deviation of RTT, which are captured from Figs. 4 and 6. Fig. 10 illustrates the RTO periods configured with the above schemes.

Fig. 11 shows the median RTT with different RTO schemes ($n = 20$). RTT improves with all RTO schemes (RTO-1 to RTO-4) in comparison to the case where molecule retransmission is disabled (RTO-0). RTO-2 yields the lowest RTT regardless of the Tx-to-Rx distance (d). Compared to RTO-0, RTO-2 improves RTT by 83,153 seconds (23 hours) when $d = 90$ μm. RTO-2 gains 1.28x speedup over RTO-0. Fig. 12 shows RTT jitter with different RTO schemes. RTT jitter improves with all RTO schemes in comparison to RTO-0. RTO-2 yields the lowest RTT jitter regardless of d. When $d = 90$ μm, RTO-2 reduces RTT jitter by 38.7 %, compared to RTO-0. Fig. 13 illustrates the rate of message transmission failure with different RTO schemes ($n = 20$). A message transmission is considered failed if a message is not delivered with up to five retransmissions. Message transmission failure rate reaches zero in all RTO schemes. In comparison, when message retransmission is disabled (Fig. 7), message transmission failure rate is over 70 % ($n = 20$ and $d = 90$ μm). Message retransmission substantially aids to decrease the failure rate.

In summary, Figs. 11, 12 and 13 demonstrate that the proposed SW-ARQ protocol successfully enhances the performance and reliability of in-sequence molecular communication in diffusive transports.

V. Conclusion

This paper considers diffusive molecular communication transports and studies a feedback-based communication protocol with the Stop-and-Wait Automatic Repeat Request (SW-ARQ) mechanism. By means of redundant molecule transmissions, molecule delivery acknowledgement and timeout-based retransmissions, the proposed protocol is designed to enhance the reliability of molecular communication. Simulation results demonstrate that the proposed protocol significantly improves the latency, jitter and transmission failure rate in in-sequence message transmissions.

References

[1] M. Pierobon and I. F. Akyildiz, "Diffusion-based noise analysis for molecular communication in nanonetworks," *IEEE Trans. Signal Process.*, vol. 59, no. 6, 2011.

[2] K. V. Srinivas, R. S. Adve, and A. W. Eckford, "Molecular communication in fluid media: The additive inverse gaussian noise channel," *IEEE Trans. Inf. Theory*, vol. 58, no. 7, 2012.

[3] T. Furubayashi, T. Nakano, A. Eckford, Y. Okaie, and T. Yomo, "Packet fragmentation and reassembly in molecular communication," *IEEE Trans. NanoBiosci.*, vol. 15, no. 3, 2016.

[4] H. O. Burton and D. D. Sullivan, "Errors and error control," *Proc. of the IEE*, vol. 60, no. 11, 1972.

[5] T. Nakano, Y. Okaie, and A. V. Vasilakos, "Transmission rate control for molecular communication among biological nanomachines," *IEEE J. Sel. Area Comm.*, vol. 31, no. 12, pp. 835–846, 2013.

[6] L. Felicetti, M. Femminella, G. Reali, T. Nakano, and A. V. Vasilakos, "TCP-like molecular communications," *IEEE J. Sel. Area Comm.*, vol. 32, no. 12, pp. 2354–2367, 2014.

[7] X. Wang, M. D. Higgins, and M. S. Leeson, "Simulating the performance of SW-ARQ schemes within molecular communications," *Simulation Modelling Practice and Theory*, vol. 42, 2014.

[8] C. Bai, M. S. Leeson, and M. D. Higgins, "Performance of SW-ARQ in bacterial quorum communications," *Nano Commun. Netw.*, vol. 6, no. 1, 2015.

[9] J. S. Mitzman, B. Morgan, T. M. Soro, J. Suzuki, and T. Nakano, "A feedback-based molecular communication protocol for noisy intrabody environments," in *17th IEEE Int'l Conference on E-health Networking Applications and Services*, 2015.

[10] M. E. Ortiz and D. Endy, "Engineered cell-cell communication via DNA messaging," *J. Biol. Eng.*, vol. 6, no. 16, 2012.

[11] Y. Erlich and D. Zielinski, "DNA fountain enables a robust and efficient storage architecture," *Science*, vol. 355, no. 6328, pp. 950–954, 2017.

[12] D. E. Smith, T. T. Perkins, and S. Chu, "Dynamical scaling of DNA diffusion coefficients," *Macromolecules*, vol. 29, 1996.

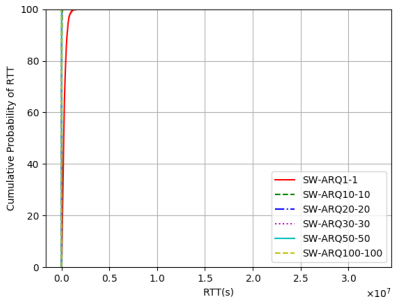

Fig. 2. RTT Probability Distribution. d=30μm. RTO=∞.

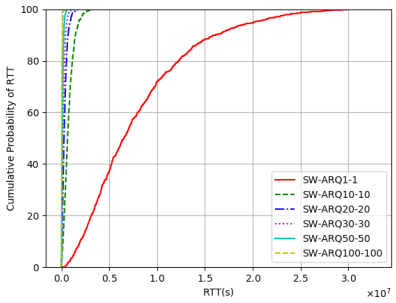

Fig. 3. RTT Probability Distribution. d=90μm. RTO=∞.

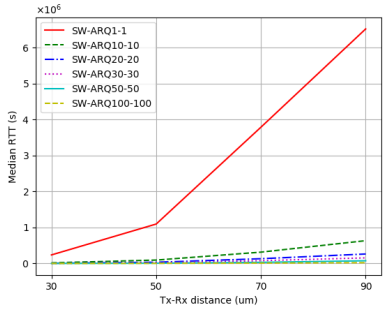

Fig. 4. Median RTT under Different Tx-Rx- distances (d). RTO=∞.

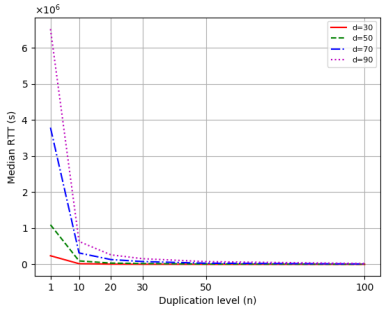

Fig. 5. Median RTT under Different Duplication Levels (n). RTO=∞.

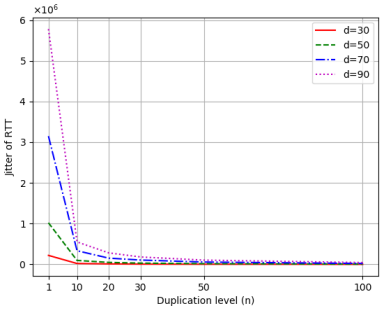

Fig. 6. RTT Jitter under Different Duplication Levels (n). RTO=∞.

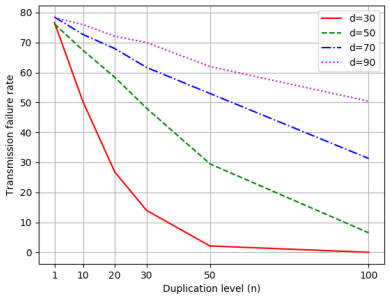

Fig. 7. Message Transmission Failure Rate (%) under Different Duplication Levels (n). RTO=∞.

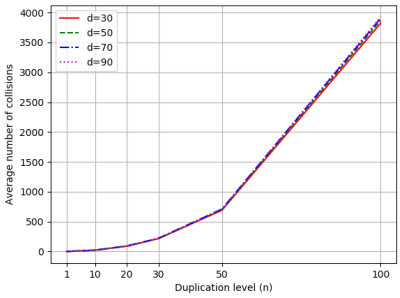

Fig. 8. Average Number of Collisions under Different Duplication Levels (n). RTO=∞.

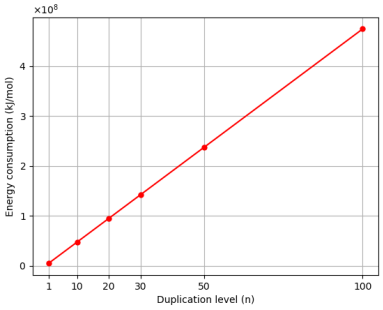

Fig. 9. Energy Consumption under Different Duplication Levels (n). RTO=∞.

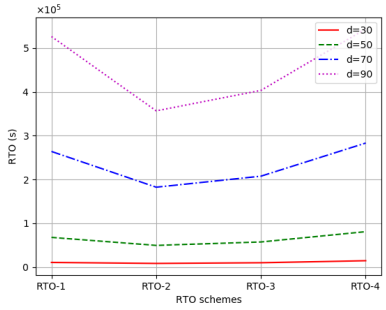

Fig. 10. Retransmission TimeOut (RTO) Periods in Different RTO Setting Schemes

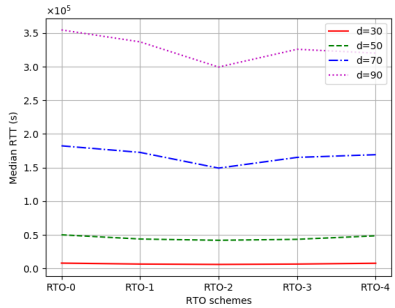

Fig. 11. Median RTT under Different RTO Schemes. RTO$\neq\infty$.

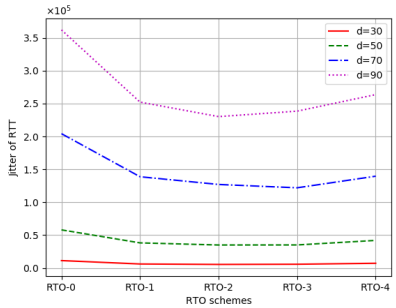

Fig. 12. RTT Jitter under Different RTO Schemes. RTO$\neq\infty$.

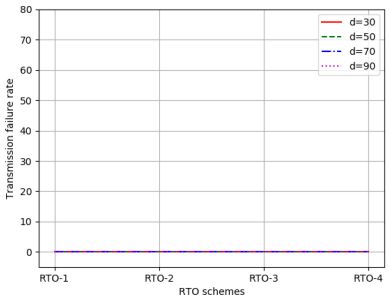

Fig. 13. Message Transmission Failure Rate under Different RTO Schemes. RTO$\neq\infty$