ベクトル場による生体組織を伝播する非線形波動の可視化

〜 心筋運動の時空ダイナミックス 〜

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はじめに本研究は統計数理研究所共同研究の研究会「医用診断のための応用統計数理の新展開」で「生体組織を伝播する非線形波動の時空ダイナミックス」の枠組みで、心室筋興奮伝播波がメカニカルな収縮力を獲得するメカニズムの解明をめざして、特に「非線形・非平衡開放系の不安定性の基礎研究」の立場から研究会の趣旨に沿って進めてきた開発途上にある成果の一部を報告するものである。

まず金井らが、高精度・高分解能の計測が可能な超音波医療診断装置を開発し[1]、収縮末期の大動脈弁閉鎖時に，大動脈弁の閉鎖にともなう力学的刺激波が心室中隔壁に沿ってパルス波状の伝播波を観測している[1]。更に，金井らは「心電図Q波からR波の間のタイミングに，自発的に発生したパルス振動が心筋を伝搬する生理学的な現象」をはじめて発見した[1]。拍動に伴う心臓の心室中隔壁の自発的な興奮伝播波を **in vivo** で計測可能とする技術は世界ではじめての画期的な発見である。　本研究の目的は正常者の心室中隔壁を伝播する速度波形を計測し、その時空間特性を位相勾配からなるベクトル場で表示し、複素ギンツブルグ・ランダウ方程式の厳密解として知られている Bekki-Nozaki ホール解と測定値を比較検討し、ホール解の存在を実験的に検証することである。位相勾配によるベクトル場表示は、可視化のための見かけ上の測定精度の向上が非線形波動の局所と大域的な情報を正確に記述できるため、波の不安定性やその現象の把握の定量化が容易になるらどの特徴のため客観的に正確な結果を導くことが出来る。最近の更に進んだ研究では正常な 21 才の男性の心室中隔壁に voltex flow が発現し時間的に進行する BN-ホールの存在を確認し検証してきた。健常者の心臓にホールが存在する事実を BN 理論と比較検討し高い精度での実験的検証にはじめて成功し既に論文として発表してきた[2]。　しかし、本発表論文には客観的に読者の立場からみて納得のいかない、問題となるいくつの中心的な課題があるので、これらを懺悔して疑いを晴らさなければならない。ここでは、これらを主題にした問題設定とその回答を正確にしておく必要がある。しかし、本研究のＪＰＳＪの注目論文として学会が推薦したことであり、実態を紹介しなければ客観的な問題をひきだせない。

そこで、これまで本研究会で実験に関しては何度かにわたり説明してきたこともあり、ここではまず後半の部分を抜粋して、おくことにしましょう。但し、本論文は合作とはいえ、筆頭者は戸次であり、殆ど筆頭者本人の纏めてあ論文に多少とも不可解なことにならないよう原文を部分的に抜粋することにして、話を進める。

これまでに先行研究では、Bekki－Nozaki Hole (BN-Hole)　の本質を理論が示した論文の一部については、いくつかの先行研究は存在するが、論文の著者や理論的解説等では、BN-Hole は散逸系の局在した dip がソリトンライクに振る舞う事実があり、これを Complex Ginzburg Landau Equation(CGLE) 方程式 の殆ど不可能と言われた厳密解を Bekki-Nozaki 論文で Hole 解の存在を世界にさきがけて、初めて見出した、数学的に難解な段階をふみ、見出した解であることはよく知られている。Hole 解で重要なことは、理論が One Parmeter Family であるため、本来、厳密解なので実験結果と比較する上で調節パラメータや data の Fitting を必要としない。実際は、初期過程で色々試行錯誤がつきまとうが、厳密解なので、Nonadjustable Parameter の理論であるので普遍的な結果をだす必要がある。従って、data を実験と比較するさい本来ならば比較したパメターが理論とコンシステントに全て合致しなければならない。BN-Hole の理論ではほゞ１０個のパラメタを比較検討しなければならず、ＢＮ－理論が謳っている１０個のコンシステントな普遍的答えを出した論文はこれまでに見受けられない。そこで、この事情にふれるために、以下に原著論文を抜粋することにした。

Bekki-Nozaki Hole in Traveling Excited Waveson Human Cardiac Interventricular Septum

Naoaki Bekki*, Yoshifumi Harada[1] and Hiroshi Kanai[2]

We observe some phase singularities in traveling excited waves noninvasively measured by a novel ultrasonic method, on a human cardiac interventricular septum (IVS) for a healthy young male. We present a possible physical model explaining a part of one-dimensional cardiac dynamics of the observed phase defects on the IVS. We show that at least one of the observed phase singularities in the excited waves on the IVS can be explained by the Bekki-Nozaki hole solution in the Complex Ginzburg-Landau Equation, although the creation and annihilation of phase singularities on the IVS give birth to a variety of complex patterns.

In this Letter, we show that at least one of the phase singularities in the excited waves on a human cardiac IVS can be explained by the Bekki-Nozaki hole solution[7] in the Complex Ginzburg-Landau Equation.

The Complex Ginzburg-Landau Equation (CGLE) [8-15] is well known for one of the simplest models that account for the behaviors of nonlinear waves and the spontaneously formed complicated patterns in the spatially extended non-equilibrium systems: the ionization waves in the glow discharge,[16] the chemical oscillations and turbulence,[17] the hydrothermal nonlinear waves in a laterally heated layer,[18] and so on. A wide class of nonlinear waves for such strong dispersive systems can be described by the one-dimensional nonlinear partial differential equation which is called CGLE,

$$i\frac{\partial}{\partial t}\psi + p\frac{\partial^2}{\partial x^2}\psi + q|\psi|^2\psi = i\gamma\psi, \tag{1}$$

where ψ is a complex function of scaled time t and space x, and with the two complex coefficients ($p = p_r + ip_i$, $q = q_r + iq_i$) and a real positive constant γ. It is noted that CGLE is represented by the full coefficients without rescaling in order to make a direct comparison between the observed data and the exact solutions of CGLE.

One of the exact solutions of CGLE connects two different patterns specified by the asymptotic wavenumbers and a phase-jump between two patterns, which is called the Bekki-Nozaki (BN) hole.[7] However, very few experimental investigations of BN hole have been reported up to now.[18, 19] The estimation of the rescaled coefficients of CGLE from the experimental data has been a difficult task, because some localized amplitude holes have been observed in the hydrothermal nonlinear waves, and not adequately compared with BN hole solution in CGLE.[18]

Let us first demonstrate a typical observation related to the phase singularities in the excited waves on the IVS for a healthy young male, as is shown in Figs. 1 ~ 3, by developing an ultrasonic noninvasive novel imaging modality with high temporal and spatial resolutions[5] which shows that the propagation of the mechanical wave-front occurs at the end of the cardiac systole by simultaneous measurement of the vibrations at many points (10,000 points) set in the IVS. We obtained two-dimensional patterns of phase and amplitude of the excited waves on the IVS : $\Theta(x, y, t)$ and $A(x, y, t) = |\tilde{\Psi}(x, y, t)|$, where x-axis denotes the Line (beam) direction and y-axis does the circumferential (depth) direction. Indeed, the observed data of phases and amplitudes demonstrate a variety of complex patterns, which include a zigzag pattern and the target waves on the IVS.[20] Our interest is, however, focussed on one-dimensional cardiac dynamics of phase singularities on the IVS, which may be viewed as a one-dimensional generalization of a core of two-dimensional target patterns.[6, 20] For the

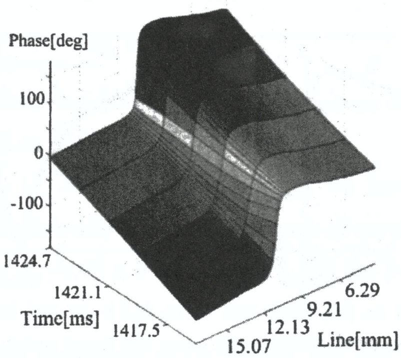


Fig. 2. (Color online) Observed local phase profile $\Theta(x, t)$ [deg] on the IVS with a phase-jump at $x_h = 10.5$[mm] in the Line direction for $1415.7 < t < 1424.7$ [ms] and $3.19 < x < 16.95$ [mm]. We can clearly observe a profile of traveling phase-jump.

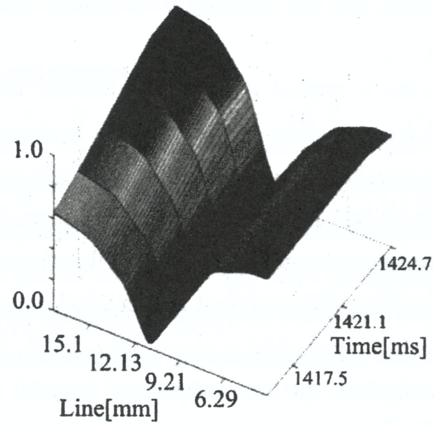


Fig. 3. (Color online) Observed amplitude profile $A(x,t)$ near the phase-jump at $x_h = 10.5$[mm] in the Line direction for $1415.7 < t < 1424.7$ [ms] and $3.19 < x < 16.95$ [mm]. We can clearly observe an amplitude-hole with phase singularity and obtain the velocity of the amplitude-hole (See eq.

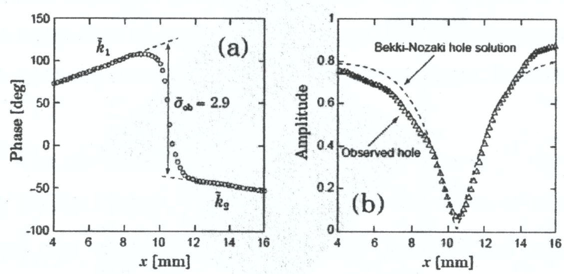


Fig. 4. (a) A snapshot of observed phase-jump near the local point $x_h = 10.5$ [mm] at a fixed time $t = 1421.1$. Circle denotes the phase of excited waves $\Theta(x,t)$ [deg]. We obtain the asymptotic wave-numbers $\tilde{k}_1 = 0.13$ [mm^{-1}], $\tilde{k}_2 = -0.05$ [mm^{-1}], and the phase-jump $\tilde{\sigma}_{ob} = 2.9$ [rad]. (b) A snapshot of observed amplitude hole and the Bekki-Nozaki (BN) hole with the coefficients $\mathfrak{C}_h$. Triangle denotes the amplitude hole $A(x,t)$ for the fixed time $t = 1421.1$. The curvature near the observed hole defined by eq. (11) is $|\tilde{\kappa}| = 0.39$ [mm^{-1}] and the curvature near BN hole is $|\kappa| = 0.4031$.

As is shown in Fig. 2, we can obtain a pair of asymptotic local wavenumbers $\tilde{k}_j (j = 1, 2)$ defined by

$$\tilde{k}_j = \frac{1}{T_2 - T_1} \int_{T_1}^{T_2} \frac{\Theta(x_2, t) - \Theta(x_1, t)}{x_2 - x_1} dt, \tag{3}$$

where $\tilde{k}_1$ for $x_1 < x_2 < x_h$ and $\tilde{k}_2$ for $x_h < x_1 < x_2$ during $T_1 < t < T_2$, respectively. A position of phase singularity (hole) is denoted by x_h, and a life-time of hole in our case is about 10 [ms] for a very slow speed of hole. We also define a phase-jump $\tilde{\sigma}_{ob}$,

$$\tilde{\sigma}_{ob} = \lim_{\epsilon \to +0} \sup_{x \in \mathbb{R}} \left| \Theta(x - x_h - \epsilon, t) - \Theta(x - x_h + \epsilon, t) \right|, \tag{4}$$

where the phase $\Theta(x, t)$ is linearly extrapolated at a fixed time. Figure 2 shows a typical one-dimensional phase $\Theta(x, t)$ [deg] at a certain small region ($3.19 < x < 16.95$ [mm] and $1415.7 < t < 1424.7$ [ms]). From Fig. 2 and eq. (4), we can observe a phase-jump $\tilde{\sigma}_{ob} = 2.9$ [rad].

Next, let us define a position x' of minimum amplitude at time t_1 and a position x'' of minimum amplitude at time t_2, then, in a uniform linear motion of phase singularities, we have its velocity $\tilde{c}_h$ [mm/ms] defined by

$$\tilde{c}_h = \frac{x'' - x'}{t_2 - t_1}. \tag{5}$$

As is shown in Fig. 3, we can observe a propagation of the phase singularity on the IVS and we have $\tilde{c}_h = -0.08$ [mm/ms] from eq. (5).

Finally, from eqs. (3) and (4), as is shown in Fig. 4, we have obtained the following fundamental physical quantities related to BN hole : (i) a pair of asymptotic local wavenumbers $\tilde{k}_1 = 0.13 \pm 0.01$ [mm^{-1}] and $\tilde{k}_2 = -0.05 \pm 0.005$ [mm^{-1}], (ii) the phase-jump $\tilde{\sigma}_{ob} = 2.9 \pm 0.1$ [rad], and the curvature defined by eq. (11) near the hole $|\tilde{\kappa}| = 0.39 \pm 0.02$ [mm^{-1}]. Here the curvature does not mean the reciprocal of its radius. On the other hand, from eq. (5), (iii) we have also obtained the velocity of phase singularity $\tilde{c}_h = -0.08 \pm 0.01$ [mm/ms] for $1415.7 < t < 1424.7$ [ms], as is shown in Fig. 3. A set of observations obtained from the data
(iii) we have also obtained the velocity of phase singularity $\tilde{c}_h = -0.08 \pm 0.01$ [mm/ms] for $1415.7 < t < 1424.7$ [ms], as is shown in Fig. 3. A set of observations obtained from the data
(2) is represented by

$$\tilde{K}_{ob} = \{\tilde{k}_1, \tilde{k}_2, \tilde{c}_h, \tilde{\sigma}_{ob}, |\tilde{\kappa}|\} \in \mathbb{R}^5. \tag{6}$$

Similarly, we have observed another traveling amplitude holes at many points in y-axis (circumferential direction) as well as in x-axis (beam direction) and two-dimensional target waves on the IVS.[20]

Solving the reality condition in the bilinear form of CGLE,[7,12] we have an important parameter α mentioned previously,

$$\alpha = -\beta \pm \sqrt{\beta^2+2} \ \ (\beta \equiv \frac{3}{2}\frac{p_r q_r + p_i q_i}{p_r q_i - p_i q_r}). \tag{7}$$

$$\mathfrak{C} = \{p_r, p_i, q_r, q_i, \gamma\} \in \mathbb{R}^5, \tag{8}$$

where $p_i < 0$ and $q_i > 0$. Algebraic condition in CGLE uniquely determines k_1, k_2, c_h, $\arg(b_2/b_1)$ and $|b_2/b_1|$ after algebraic manipulations.

The velocity of propagating BN hole is given by

$$c_h = \frac{p_r q_i - p_i q_r}{q_i}(k_1 + k_2). \tag{9}$$

We have a phase-jump ($0 \le \sigma \le 2\pi$)

$$\begin{aligned} \sigma &\equiv \arg[\frac{b_2}{b_1}] \\ &= \arctan\left[\frac{2\frac{p_i}{q_i}\left\{(p_r q_i - p_i q_r) + \frac{1}{\alpha}(p_r q_r + p_i q_i)\right\}\kappa_+\kappa_-}{\left(\frac{p_i}{q_i}\right)^2 |q|^2\kappa_+^2 - \left(1+\frac{1}{\alpha^2}\right)|p|^2\kappa_-^2}\right]. \end{aligned} \tag{10}$$

where $\kappa_\pm = k_1 \pm k_2$. It is noted that this phase-jump connects discontinuously two different patterns specified by wavenumbers k_1 and k_2.

The curvature near the hole is given by

$$\kappa = -\kappa_-/(2\alpha). \tag{11}$$

We also obtain analytically the ratio

$$\left|\frac{b_2}{b_1}\right| = \left[\frac{(s_1+s_2)^2 + (t_1-t_2)^2}{(s_1-s_2)^2 + (t_1+t_2)^2}\right]^{\frac{1}{2}}, \tag{12}$$

where

$$s_1 = p_i\kappa_+, s_2 = \left(\frac{p_r}{\alpha} - p_i\right)\kappa_-, t_1 = p_i\frac{q_r}{q_i}\kappa_+, t_2 = (p_r + \frac{p_i}{\alpha})\kappa_-.$$

Asymptotic wavenumbers k_1 and k_2 satisfy

$$\frac{(\kappa_+)^2}{a_1^2} + \frac{(\kappa_-)^2}{a_2^2} = 1, \tag{13}$$

$$a_1^2 = \frac{4K_m^2}{1 + \dfrac{3\alpha p_i |q|^2}{(1+\alpha^2) q_i (p_r q_i - p_i q_r)}},$$

$$a_2^2 = \frac{4K_m^2}{1 + \dfrac{3 q_i |p|^2}{\alpha p_i (p_r q_i - p_i q_r)}},$$

where a_1^2 and a_2^2 are positive constants on account of the real condition and $K_m = \sqrt{\gamma/(-p_i)}$ $(p_i < 0)$.

The Bekki-Nozaki hole solution[7] is given by

$$\psi(x,t) = \frac{b_1 \exp(\kappa\xi) + b_2 \exp(-\kappa\xi)}{\exp(\kappa\xi) + \exp(-\kappa\xi)} \times \exp\left[\frac{i}{2}\int^{\xi}(\kappa_+ + \kappa_- \tanh \kappa x)dx - i\Omega t\right], \tag{14}$$

where $\xi = x - c_h t$ and $\Omega = p_r K_m^2 - c_h(k_1 k_2 + K_m^2)/(k_1 + k_2)$. Equations (9) and (13) give the algebraic relation between the velocity (c_h) and the asymptotic wavenumbers of BN hole solution with $\mathfrak{C}$. It is noted that the family of BN hole solution can be parametrized by the velocity of BN hole, as is shown in Fig. 5.

Also, equation (14) gives the following inequality

$$\frac{|b_1|^2}{4}\mathrm{sech}^2(\kappa\xi)\Big[\exp(\kappa\xi) - \left|\frac{b_2}{b_1}\right|\exp(-\kappa\xi)\Big]^2 \leqq |\psi|^2 \leqq \frac{|b_1|^2}{4}\mathrm{sech}^2(\kappa\xi)\Big[\exp(\kappa\xi) + \left|\frac{b_2}{b_1}\right|\exp(-\kappa\xi)\Big]^2. \tag{15}$$

We have observed two different patterns specified wavenumbers $\tilde{k}_1$ and $\tilde{k}_2$ near the phase defect, and the phase-jump between two patterns. The phase-jump occurs at $x_h = 10.5$[mm], as is shown in Fig. 2 and Fig. 3. the amplitude $A(x,t) = |\psi(x,t)|$ of excited waves decreases and forms a dip shaped like a hole. In order to make a direct comparison between the observed data and the exact solutions of CGLE. we must find a set of all the coefficients in CGLE.

taking into account the Benjamin-Feir instability.[14] Finally, we find all the coefficients in CGLE after much trial and error[7]

$$\mathfrak{C}_{\mathfrak{h}} = \{-1.8, -2.0, 0.5, 1.2, 0.8\}. \tag{16}$$

Let us show numerically that a set of data of BN hole solution (K_{BN}) is almost equivalent to that of $\tilde{K}_{ob}$. From eqs. (7) and (15), we have $\alpha = 0.228$. Since a pair of wavenumbers k_1 and k_2 is chosen so that eq. (13) is satisfied, as is shown in Fig. 5 (a), we can obtain $k_1 = 0.133$ and $k_2 = -0.051$. Therefore, from eq. (9), we obtain the velocity of BN hole $c_h = -0.0793$. It is noted that the selection of wavenumber occurs so that the phase-jump turns into BN hole. From eq. (11), we have the curvature near BN hole $|\kappa| = 0.4031$, as is shown in Fig. 4 (b). Substituting these parameters obtained above into eq. (10), we obtain $\sigma = 2.983$ [rad], as is shown in Fig. 5 (b). From eq. (12), we have also $|b_2/b_1| = 1.02$. As is shown in Fig. 5, we can obtain consistently K_{BN}:

$$K_{BN} = \tilde{K}_{ob}. \tag{17}$$

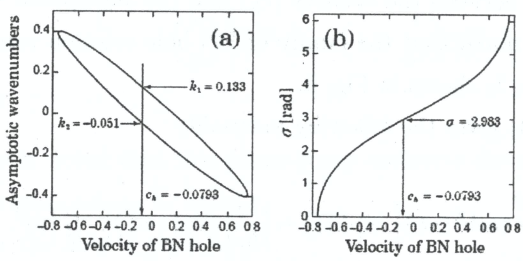
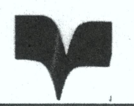
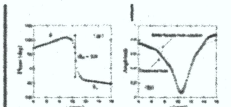
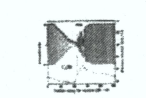
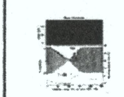
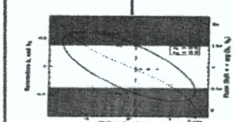
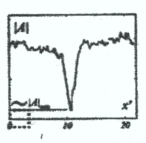
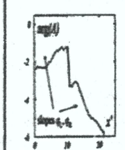
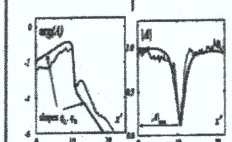
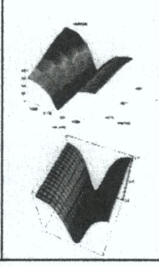
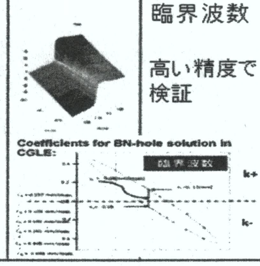


Fig. 5. (a) Asymptotic wavenumbers k_1 and k_2 versus the velocity (c_h) of BN hole ($-0.5 < k_1 (or\ k_2) < 0.5$ and $-0.8 < c_h < 0.8$). From the analytic form of BN hole solution, we obtain $k_1 = 0.133$, $k_2 = -0.051$ and $c_h = -0.0793$, respectively. We have $\kappa_+ (= k_1 + k_2) = 0$ in case of $c_h = 0$. (b) Phase-jump (σ) versus the velocity (c_h) of BN-hole ($0 \leqq \sigma \leqq 2\pi$ and $-0.8 < c_h < 0.8$). From eqs. (7) to (13) with the coefficients $\mathfrak{C}_{\mathfrak{h}}$, we can obtain the value of the phase-jump $\sigma = 2.983$ [rad] for $c_h = -0.0793$. We have $\sigma = \pi$ in case of $c_h = 0$.

Although it is difficult to estimate all the coefficients in CGLE from the observed data, we found all the corresponding coefficients in our case. Substitution of these coefficients into eq. (15) gives an amplitude profile of BN hole as in Fig. 4 (b). Different boundary condition of observed holes from BN hole explains the large deviation from BN hole for $|\kappa\xi| \gg 1$ since we can observe BN holes only in local finite small regions on the IVS. Thus, we have shown that at least one of the observed phase singularities in the excited waves on the IVS can be explained by BN hole solution of CGLE with the coefficients $\mathfrak{C}_{\mathfrak{h}}$.

A variety of complex patterns of phase-defects on the IVS except for observations of amplitude holes will be published elsewhere.[20]

先行研究

	$\tilde{K}_{\text{ob}}$ K_{BN} $\mathfrak{C}_{\text{ob}}$ $\mathfrak{C}_{\text{BN}}$			
①	検証 なし × 1) B.Janiaud, S.Jucquois, and V.Croquette, "Experimental Evidence of Bekki Nozaki Holes", Edited By S. KAI, World Scientific. (1991) 538.			
②	検証 なし × 2) J. Burguete, H. Chate´, F. Daviaud, and N. Mukolobwiez: Phys. Rev.Lett. 82 (1999) 3252.			
③ 検証 ○	3) N. Bekki, Y. Harada, and H. Kanai; "Bekki-Nozaki Hole in Traveling Excited Waves on Human Cardiac Interventricular Septum" J. Phys. Soc. Jpn. 81 (2012) 073801. $\mathfrak{C} = \{p_r, p_i, q_r, q_i, \gamma\} \in \mathbb{R}^5,$ $\mathfrak{C}_{\mathfrak{h}} = \{-1.8, -2.0, 0.5, 1.2, 0.8\}.$ $\tilde{K}_{\text{ob}} = \{\tilde{k}_1, \tilde{k}_2, \tilde{c}_h, \tilde{\sigma}_{\text{ob}}, \lvert\tilde{\kappa}\rvert\} \in \mathbb{R}^5.$			臨界波数 高い精度で検証 

$K_{\text{BN}} \cong \tilde{K}_{\text{ob}}$ $\tilde{k_1} = 0.13 \pm 0.01 mm^{-1}$, $\tilde{k_2} = -0.05 \pm 0.005\ mm^{-1}$,

$\tilde{\sigma}_{\text{ob}} = 2.9 \pm 0.1$ rad, $\tilde{c}_h = -0.08 \pm 0.01$ mm/ms $\tilde{\kappa} = 0.39 \pm 0.02\ mm^{-1}$.

最後に本研究が成功したキーポイントは４研究機関の共同研究であり、本研究会報告のくだりにある、東北大金井研の優れた測定技術と多数の研究成果、更に原田と元アロカ研究所の技術者とが開発してきたソフト資源から生まれた測定技術に負うところが大きく研究成果向上に貢献してきたことを特に言及しておきたい。限られた紙面で詳細な議論の展開が困難なため、当日の講演時にゆずり、以上本研究の成果は、**ＪＰＳＪ**に最近の注目論文として学会からの推薦があったことを付け加え概要報告としたい。

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[2] N. Bekki, Y. Harada, and H. Kanai, J. Phys. Soc. Jpn. 81 (2012)073801.