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Communications in Nonlinear Science and Numerical Simulation 111 (2022) 106462

Contents lists available at ScienceDirect

Communications in Nonlinear Science and Numerical Simulation

journal homepage: www.elsevier.com/locate/cnsns

Research paper

# Poincaré model shows how heterogeneity in light sensitivity can alter circadian clock function

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ARTICLE INFO

*Article history:*
Received 17 July 2021
Received in revised form 26 December 2021
Accepted 21 March 2022
Available online 25 March 2022

*MSC:*
92B25
34C15
05C82

*Keywords:*
Heterogeneity
Light sensitivity
Circadian rhythm
Network

ABSTRACT

Exposed to the natural light-dark cycle, living beings show robust 24 h rhythms in physiology and behavior. Interestingly, even in the absence of a light-dark cycle, for example in constant conditions, such as under the constant darkness or the constant light, living beings maintain a robust rhythm of which the endogenous period (named free running period, FRP) is close to 24 h. The endogenous rhythms are regulated by a master clock located in the suprachiasmatic nucleus (SCN) of mammals, where the SCN neurons show heterogeneity in the sensitivity to the light. In this article, we examined how this heterogeneity influences the FRP under constant light. Using a Poincaré model for the SCN network it is shown that the FRP increases with the increase of the degree of heterogeneity in the sensitivity of neuronal subpopulations to light. Moreover, the presence of a critical value where the periods of the subpopulation diverge, presents a mechanism dictating how some animals remain rhythmic under constant light conditions, while others lose their rhythms completely. Our findings help to understand how the neuronal heterogeneity to light sensitivity in the SCN influences the circadian behavior of the animal.



## 1. Introduction

Circadian rhythms are present in the behavioral and physiological activities when living beings are exposed to the natural light-dark cycle [1–6]. Interestingly, living beings maintain a robust endogenous rhythm with an period close to 24 h even in the absence of an external light-dark cycle [7–10]. In these constant conditions Aschoff's rule applies, stating that for nocturnal animals the period increases when the light intensity increases, if the light is on constantly [11–15]. The period in constant conditions is called the free running period (FRP). This FRP varies among species, and is roughly distributed between 22 h and 28 h [3].

The FRP is related to the ability to entrain to the external 24 h light-dark cycle dictated by the rotation of the earth. Individual animals, or animal species where the endogenous rhythm deviates more from 24 h also experience more difficulties to entrain to these external rhythms of 24 h in light and darkness [16,17]. For example, human chronotypes differ in their ability to adjust to the external light-dark cycle. Morning persons have an endogenous period closer to 24 h than evening persons, and evening persons have more difficulties adjusting their rhythms to the natural 24 h cycle [16].

In mammals, this clock that creates these endogenous rhythms is located in the suprachiasmatic nucleus (SCN) above the optic chiasm in the brain [5]. The SCN is composed of about 20,000 self-oscillating neurons with nonidentical intrinsic

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https://doi.org/10.1016/j.cnsns.2022.106462
1007-5704/

periods. These nonidentical neurons form a heterogeneous network that is coupled through neurotransmitters. [5,18–22], i.e., vasoactive intestinal polypeptide (VIP), arginine vasopressin (AVP), and gamma-aminobutyric acid (GABA) [23–27]. This heterogeneous network in the SCN creates a robust rhythmic output signal with a uniform circadian period. The SCN can be divided into two distinct subgroups, namely, a ventrolateral part (VL) and a dorsomedial part (DM), which differ both functionally and physiologically.

Another division involves the light-sensitivity of the neurons: approximately 25%–30% of the neurons are directly sensitive to light-information coming from the retina through the retino-hypothalamic tract (RHT), while the remaining group of neurons are insensitive to light. Until recently it was thought that the group of SCN neurons that are sensitive to the light-information are mainly situated in the VL, and the group of neurons that are not sensitive to the light input signal are situated in the DM. The coupling between the VL and the DM is asymmetrical, since the VL relays the light-information to the DM but the DM affects the VL to a lesser extend [24,28–30]. However, recently, it was reported that the light-sensitive neurons are not located in one specific subregion of the SCN [31,32]. In other words, neurons located in both VL and DM can be directly sensitive to the light information. Interestingly, one study implied that the neurons in the VL can be activated at lower light levels whereas the neurons in the DM require higher light intensities [31,32], indicating that the sensitivity to light information for the SCN neurons is heterogeneous, i.e., the sensitivity to light-information coming from the RHT is larger in the VL than in the DM [33].

We will examine whether the FRP is affected by the heterogeneity in light-sensitivity based on a Poincaré model exposed to constant light. For simplicity, the light-sensitivity for the neurons is assumed to be identical within each subregion, but is heterogeneous across different subregions. The rest of this article is organized as follows. In Section 2, the Poincaré model is introduced to simulate a SCN network exposed to the constant light. In Section 3, we present the simulation results of the effect of the heterogeneity on the FRP. In Section 4, the analytical results are presented. Finally, the conclusion and discussion are included in Section 5.

## 2. Description of Poincaré model

The Poincaré model is often used to describe the SCN neuronal network, because of its general oscillator description based on phase and amplitude, which also makes it more straightforward to perform theoretical analysis on this model [4,10,17,34,35]. Each Poincaré oscillator contains amplitude and phase information, denoted by two variables, $x$ and $y$. All oscillators are coupled through a mean field $F$. In this article, this model is used to investigate the effect of heterogeneity in light sensitivity on the FRP of the SCN. The SCN network exposed to constant light can be modeled as follows:

$$\begin{aligned}
\dot{x}_i &= \gamma x_i(a - r_i) - \frac{2y_i\pi}{\mu_i\tau} + GF + L_i,\\
\dot{y}_i &= \gamma y_i(a - r_i) + \frac{2x_i\pi}{\mu_i\tau}, \quad i = 1, 2, \ldots, N,\\
F &= \frac{1}{N}\sum_{i=1}^{N} x_i,
\end{aligned} \tag{1}$$

where $i$ denotes $i$th oscillator, the parameters $\gamma$, $a$, and $\tau$ are the relaxation parameter, intrinsic amplitude and intrinsic period of the individual oscillator, respectively. $\mu_i$ introduces the difference in the intrinsic periods for the individual oscillators which satisfies a normal distribution with the mean equal to 1 and the standard deviation $\sigma$. The parameters $G$, $L_i$, and $N$ represent cellular coupling strength, light term and the total number of the SCN neurons, respectively. The parameter $r_i$ is the amplitude of $i$th oscillator which reads

$$r_i = \sqrt{x_i^2 + y_i^2}, \quad i = 1, 2, \ldots, N. \tag{2}$$

Let the light term $L_i$ be $l_iL$, where $L$ is the intensity of the constant light and $l_i$ is the sensitivity to the light for the neuron $i$. For simplicity, we assume that the values of $l_i$ are the same for the neurons within the same subregion of the SCN and the values differ between distinct subregions. If the neuron $i$ is located in the VL (i.e., $0 < i \le N_1$), we set $l_i = 1 + q$, and if the neuron $i$ is located in the DM (i.e., $N_1 < i \le N$), we set $l_i = \frac{N - N_1(1+q)}{N - N_1}$ since $l_i$ satisfies $\frac{1}{N}\sum_{i=1}^{N} l_i = 1$. Because the sensitivity is larger for VL than for DM, we only consider the case where $q$ is larger than or equal 0. For example, when the numbers of VL neurons and DM neurons are the same (i.e., $N_1 = N_2 = \frac{N}{2}$), we obtain $l_i = 1 + q$ for the VL and $l_j = 1 - q$ for the DM, where $0 \le q \le 1$. The key parameter $q$ represents the heterogeneity degree of the light sensitivity for the VL neurons and DM neurons. If $q = 0$, the light sensitivity is the same between these two groups. If $q > 0$, there is heterogeneity in the sensitivity to light between both groups.

In the present study, we used the fourth order Runge–Kutta method with time steps of 0.01 h for the numerical simulations. The initial 5,000,000 steps were neglected to avoid the effect of transients and the next 100,000 steps were selected. The initial values of $x$ and $y$ were selected randomly from a uniform distribution in (0,1) for each oscillator. The parameter $\gamma$ is the rigidity of the oscillatory system, which represents the stability of the system with respect to amplitude perturbations (amplitude relaxation rate upon perturbation) [4,36]. In Refs. [4,37] $\gamma$ is set to be 1, because the

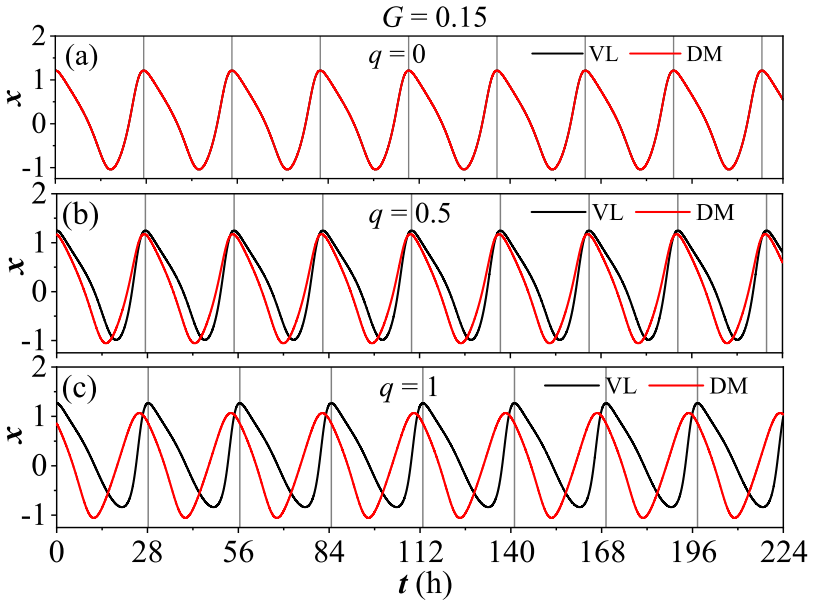


**Fig. 1.** Temporal evolutions of one VL neuron and one DM neuron affected by the heterogeneity degree $q$ under the constant light. $q = 0.0$ in (a), $q = 0.5$ in (b) and $q = 1$ in (c). It is visible that the FRP increases with the increase of $q$. The peak of the VL neuron is indicated by a black solid line, thus, the FRP is the intervals between two consistent solid lines. The coupling strength is $G = 0.15$. Note that the neurons within one subgroup are identical, therefore, we select one VL neuron or one DM neuron to present the VL subgroup or the DM subregion, respectively.

SCN was regarded as a rigid oscillator, as opposed to peripheral oscillators that have a smaller value for $\gamma$. The particular value of the amplitude relaxation rate $\gamma = 1$ is comparable with experimental measurement [4,37]. Because the exact value of neuronal amplitude cannot be found now, in experiments, for simplicity, the intrinsic neuronal amplitude $a$ is set to be 1 [4]. The parameter $\tau$ is the intrinsic period of the neurons which is close to the external day–night period, and consequently, it is set to be 24 h [4]. Accordingly, we set $\gamma = 1$, $a = 1$, $\tau = 24$ throughout the article. The coupling strength $G$ is selected to be around 0.1 [4,30]. If $G$ = 0.2, the endogenous period of the SCN network is about 40 h which is far away from 24 h. Therefore, we here select $G$ as 0.05, 0.1, or 0.15. There is no evident to show whether the coupling effect is larger than light effect or vice versa, consequently, the light intensity is select as 0.1, i.e., three cases are examined in the present study, $G > L$, $G = L$ and $G < L$, respectively. Without special statement, the standard deviation is $\sigma = 0$, the total number of neurons was $N = 100$, of which the number for the VL neurons was $N_1 = 50$ and for the DM neurons was $N_2 = 50$.

## 3. Numerical results

An illustrative example for the effect of heterogeneity degree in light sensitivity $q$ on the FRP is shown in Fig. 1. If the degree equals 0, the light sensitivity of the neurons in both SCN regions is identical (i.e., homogeneous throughout the SCN), no phase difference between the VL and the DM is found (Fig. 1a). Thus, the VL and the DM are perfectly synchronized, with equal periods of about 27.2 h. With $q = 0.5$ (Fig. 1b), the sensitivity to light is three times higher in VL than in DM. In this case, VL and DM are still synchronized, but with a moderate but fixed phase difference. The periods of both VL and DM oscillators are about 27.4 h. With $q = 1$ (Fig. 1c), the neurons in the DM region are not sensitive to light at all, and only neurons in the VL are sensitive to light. The VL and the DM remain synchronized, but the phase difference is somewhat larger, but still fixed. The periods of both subgroups are around 28.2 h. Therefore, with the increase of the heterogeneity degree $q$, the free-running period (FRP) of the SCN increases.

Next, the heterogeneity in light-sensitivity in the SCN regions was investigated for different coupling strengths between both regions. Fig. 2 shows the quantitative relationship of the FRP for each subregion to the heterogeneity degree $q$ for three selected cases of coupling strength. The coupling strength is $G = 0.05, 0.1$ and 0.15 from panel (a) to panel (c), respectively. For weak coupling strengths, in (a) and (b), a critical value is observed where the periods of the VL and DM regions disperse when $q$ is larger than this critical value $q_c$, and the synchronization between the regions is lost, because the period of VL increases with increasing $q$, and the period of DM decreases with increasing $q$. When $q$ is not larger than $q_c$, the FRP of the VL and the FRP of the DM are equal and increase with the increase of $q$ (see inset in both panels). The critical value for $G = 0.05$ is $q_c = 0.33$ and for $G = 0.1$ is $q_c = 0.68$, respectively. In (c), when the coupling strength is large, the periods of the VL and the DM are equal in the whole investigated range of $q$, which increases with the increase of $q$. Therefore, $q$ influences the FRP of the SCN as well as the synchronization between these two subregions.

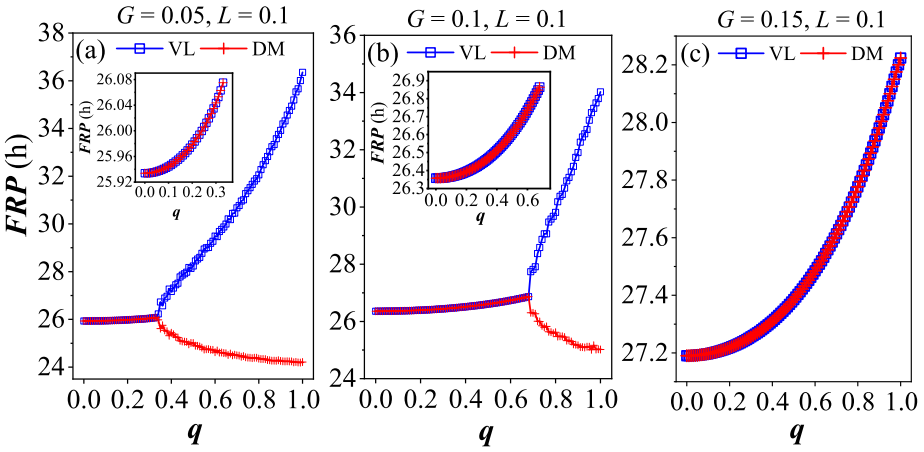


**Fig. 2.** The relationship of the FRP for each subregion to the heterogeneity degree $q$ with selected coupling strength. The coupling strength is $G = 0.05, 0.1, 0.15$ from (a) to (c), respectively, and the intensity of the constant light $L$ is 0.1. In the inset in (a) or (b), the relationship for $q < q_c$ is enlarged to show that the period increases for increasing $q$.

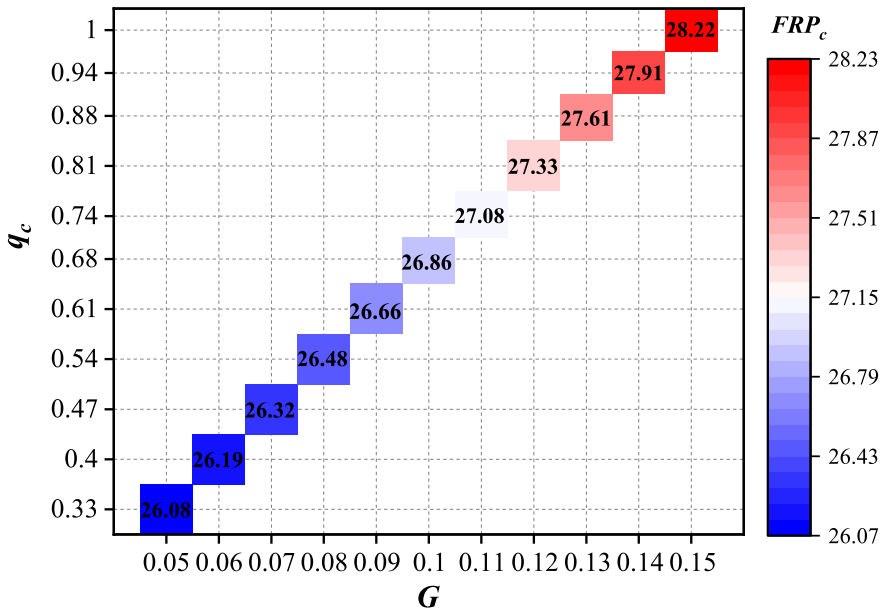


**Fig. 3.** The relationship of the critical value $q_c$ of the heterogeneity degree or the critical free running period $FRP_c$ to the coupling strength $G$. The coupling strength $G$ is selected from 0.05 to 0.15 with interval 0.01, and the intensity of the constant light $L$ is 0.1.

The relationship of the FRP for each subregion to the heterogeneity degree $q$ with selected coupling strength $G$ = 0.07, 0.09 and 0.11 is shown in Fig. S1 in the supplementary materials. These findings are consistent with Fig. 2.

Moreover, we examined the relationship of the critical value $q_c$ of the heterogeneity degree or the critical free running period $FRP_c$ to the coupling strength $G$ in Fig. 3. It follows that with the increase of the coupling strength $G$, both $q_c$ and $FRP_c$ increase.

We examined whether the network structure of the SCN affects the main results. Two network types are considered, the small-world network [21,22,38] and completely random network [38]. The relationship of the FRP for each subregion to the heterogeneity degree $q$ on the small-world and completely random network is shown in Figs. S2 and S3, respectively, in the supplementary materials. These findings are also consistent with Fig. 2.

In addition, we examined whether the difference in the neuronal intrinsic periods affects the relationship between the FRP for each subgroup and the heterogeneity degree in light-sensitivity $q$ (Fig. 4). It is visible that the relationship is not alternated by the deviation $\sigma$ qualitatively. In other words, the relationship remains positive between the FRP and $q$ when $q < q_c$ in (a) and (b) or in the whole investigated range of $q$ in (c) for all intrinsic neuronal periods.

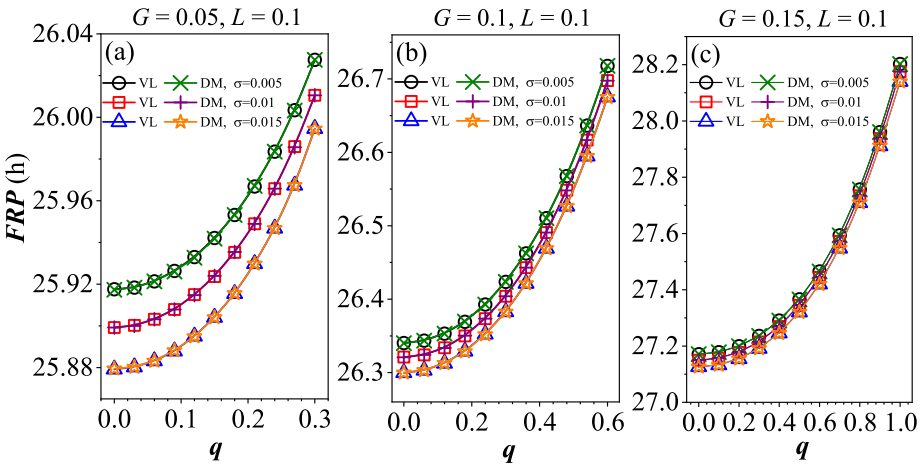


**Fig. 4.** The relationship of the FRP for each subgroup to the heterogeneity degree $q$ when the neuronal intrinsic periods differ. The deviation is selected as $\sigma = 0.005, 0.01$, and $0.015$, respectively, and the intensity of the constant light $L$ is 0.1. (a) and (b) corresponds to the insets of (a) and (b) in Fig. 2, respectively, and (c) to (c) in Fig. 2.

## 4. Analytical results

To simplify the analysis, we set $N = 2$, i.e., one oscillator represents the VL and the other represents the DM. The mean field is reduced to $F = \frac{x_1+x_2}{2}$. Accordingly, Eq. (1) can be rewritten as

$$\begin{aligned}
\dot{x}_1 &= \gamma x_1(a - r_1) - \frac{2y_1\pi}{\tau} + \frac{x_1 + x_2}{2}G + L_1,\\
\dot{y}_1 &= \gamma y_1(a - r_1) + \frac{2x_1\pi}{\tau},\\
\dot{x}_2 &= \gamma x_2(a - r_2) - \frac{2y_2\pi}{\tau} + \frac{x_1 + x_2}{2}G + L_2,\\
\dot{y}_2 &= \gamma y_2(a - r_2) + \frac{2x_2\pi}{\tau},
\end{aligned} \tag{3}$$

where $L_{1,2} = l_{1,2}L$. For convenience, we convert Eq. (3) from Cartesian coordinates to polar coordinates. Let $x_1 = r_1\cos\theta_1, y_1 = r_1\sin\theta_1, x_2 = r_2\cos\theta_2, y_2 = r_2\sin\theta_2$, and $\omega = \frac{2\pi}{\tau}$. After substitute them into Eq. (3), one can obtain

$$\begin{aligned}
\dot{r}_1 &= \gamma r_1(a - r_1) + (r_1\cos^2\theta_1 + r_2\cos\theta_1\cos\theta_2)\frac{G}{2} + L_1\cos\theta_1,\\
\dot{\theta}_1 &= \omega - (r_1\cos\theta_1\sin\theta_1 + r_2\cos\theta_2\sin\theta_1)\frac{G}{2r_1} - \frac{L_1}{r_1}\sin\theta_1,\\
\dot{r}_2 &= \gamma r_2(a - r_2) + (r_2\cos^2\theta_2 + r_1\cos\theta_1\cos\theta_2)\frac{G}{2} + L_2\cos\theta_2,\\
\dot{\theta}_2 &= \omega - (r_1\cos\theta_1\sin\theta_2 + r_2\cos\theta_2\sin\theta_2)\frac{G}{2r_2} - \frac{L_2}{r_2}\sin\theta_2.
\end{aligned} \tag{4}$$

When the oscillators are synchronized, let $\theta_1 = \Omega t + \phi_1$ and $\theta_2 = \Omega t + \phi_2$ and $\alpha = \phi_2 - \phi_1$, where $\Omega$ is the angular frequency. The averaging method developed by Krylov and Bogoliubov as used in Ref. [4,39–41] is taken into account, then we have

$$\begin{aligned}
&\langle\cos^2(\phi_1 + \Omega t)\rangle = \frac{1}{2},\\
&\langle\cos(\phi_2 + \Omega t)\cos(\phi_1 + \Omega t)\rangle = \frac{\cos\alpha}{2},\\
&\langle\cos(\phi_1 + \Omega t)\sin(\phi_1 + \Omega t)\rangle = 0,\\
&\langle\cos(\phi_2 + \Omega t)\sin(\phi_1 + \Omega t)\rangle = -\frac{\sin\alpha}{2},\\
&\langle\cos(\phi_1 + \Omega t)\sin(\phi_2 + \Omega t)\rangle = \frac{\sin\alpha}{2},
\end{aligned} \tag{5}$$

where $\langle\cdot\rangle$ represents the average in one circadian cycle. If the VL and DM output one uniform FRP, we obtain $\dot{r_1} = \dot{r_2} = 0$, $\dot{\theta_1} = \dot{\theta_2} = \Omega$. For simplicity, the non-averaged sign of $r_1$, $r_2$, $\phi_1$ and $\phi_2$ is kept in the following. Substituting Eq. (5) into Eq. (4), Eq. (6) is obtained

$$\begin{aligned} 0 &= \gamma r_1(a - r_1) + (r_1 + r_2\cos\alpha)\frac{G}{4} + L_1\cos\theta_1, \\ \Omega &= \omega + \frac{r_2 G\sin\alpha}{4r_1} - \frac{L_1}{r_1}\sin\theta_1, \\ 0 &= \gamma r_2(a - r_2) + (r_1\cos\alpha + r_2)\frac{G}{4} + L_2\cos\theta_2, \\ \Omega &= \omega - \frac{r_1 G\sin\alpha}{4r_2} - \frac{L_2}{r_2}\sin\theta_2. \end{aligned} \tag{6}$$

From Eq. (6), we obtain

$$\begin{aligned} \cos\theta_1 &= \frac{r_1(a - r_1) + (r_1 + r_2\cos\alpha)\frac{G}{4}}{-L_1}, \\ \sin\theta_1 &= \frac{r_1(\omega + \frac{r_2 G\sin\alpha}{4r_1} - \Omega)}{L_1}, \\ \cos\theta_2 &= \frac{r_2(a - r_2) + (r_2 + r_1\cos\alpha)\frac{G}{4}}{-L_2}, \\ \sin\theta_2 &= \frac{r_2(\omega - \frac{r_1 G\sin\alpha}{4r_2} - \Omega)}{L_2}. \end{aligned} \tag{7}$$

Because of $\sin^2\theta_1 + \cos^2\theta_1 = 1$, and $\sin^2\theta_2 + \cos^2\theta_2 = 1$, Eq. (7) is simplified as

$$\begin{aligned} &[\frac{r_1(a - r_1) + (r_1 + r_2\cos\alpha)\frac{G}{4}}{-L_1}]^2 + [\frac{r_1(\omega + \frac{r_2 G\sin\alpha}{4r_1} - \Omega)}{L_1}]^2 = 1, \\ &[\frac{r_2(a - r_2) + (r_2 + r_1\cos\alpha)\frac{G}{4}}{-L_2}]^2 + [\frac{r_2(\omega - \frac{r_1 G\sin\alpha}{4r_2} - \Omega)}{L_2}]^2 = 1. \end{aligned} \tag{8}$$

When the oscillators are synchronized, Fig. 5 shows the amplitudes of the VL and DM are almost equal ($R \equiv r_1 \approx r_2$). Therefore, from Eq. (8) we obtain

$$\sin\alpha = \frac{4qL^2}{R^2 G(\omega - \Omega)}, \tag{9}$$

where $L_1 = (1 + q)L$, $L_2 = (1 - q)L$.

When the VL and DM output one uniform FRP, i.e., the oscillators are synchronized, the difference between the VL and the DM is very small in that we obtain $\alpha \to 0$ and $\cos\alpha \to 1$. After substitute Eq. (9) into Eq. (8), one can obtain

$$b^2 + R^2[\omega + \frac{qL^2}{R^2(\omega - \Omega)} - \Omega]^2 = (1 + q)^2 L^2, \tag{10}$$

where

$$b \equiv R(a - R) + \frac{GR}{2}. \tag{11}$$

Therefore, $\Omega$ can be solved from Eq. (10):

$$\Omega = \omega - [\frac{\sqrt{(1 + q)^2 L^2 - b^2}}{2R} - \frac{\sqrt{(1 - q)^2 L^2 - b^2}}{2R}]. \tag{12}$$

If $q$ is a small value, Eq. (12) is altered to be

$$\Omega \approx \omega - \frac{L^2}{R\sqrt{L^2 - b^2}}q. \tag{13}$$

From Eq. (13), we observe that the relationship between $\Omega$ and $q$ is negative, i.e., between FRP and $q$ is positive. This means that, when the VL and the DM are synchronized, the FRP of the VL and the FRP of the DM are equal and increase with the increase of $q$. Consequently, we theoretically explain the results in Fig. 2.

From Eq. (12), the range of the heterogeneity degree $q$ can be obtained, i.e., $0 \le q \le 1 - \frac{b}{L}$, therefore, the critical value of the heterogeneity degree is

$$q_c = 1 - \frac{b}{L}. \tag{14}$$

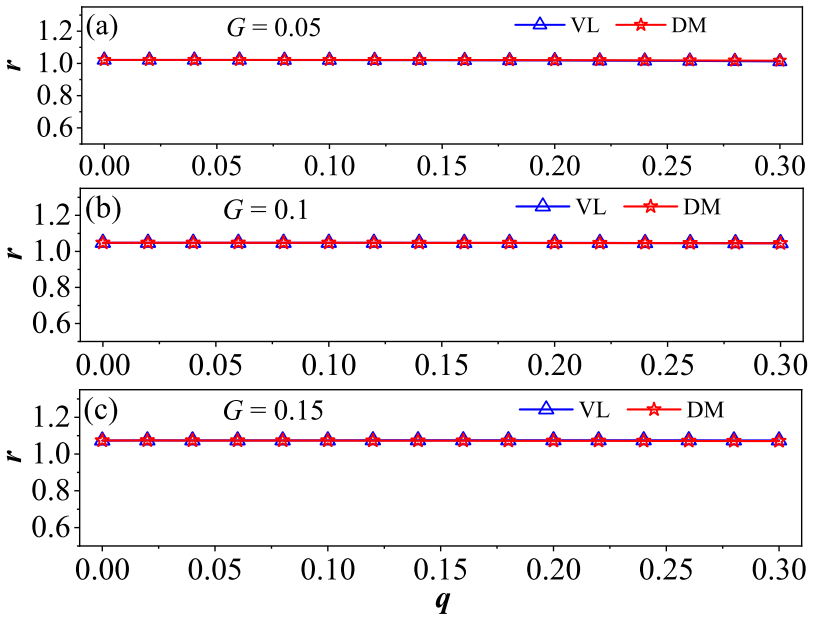


**Fig. 5.** The neuronal amplitudes $r$ of each subgroup versus the degree $q$ when the SCN neurons are synchronized. The coupling strength $G$ is 0.05, 0.1, 0.15 in (a–c), respectively. $r_{VL}$ and $r_{DM}$ is $r_1$ and $r_2$ respectively, $R \equiv r_1 \approx r_2$. These figures are simulated based on Eq. (1), and the parameters are the same as for Fig. 2.

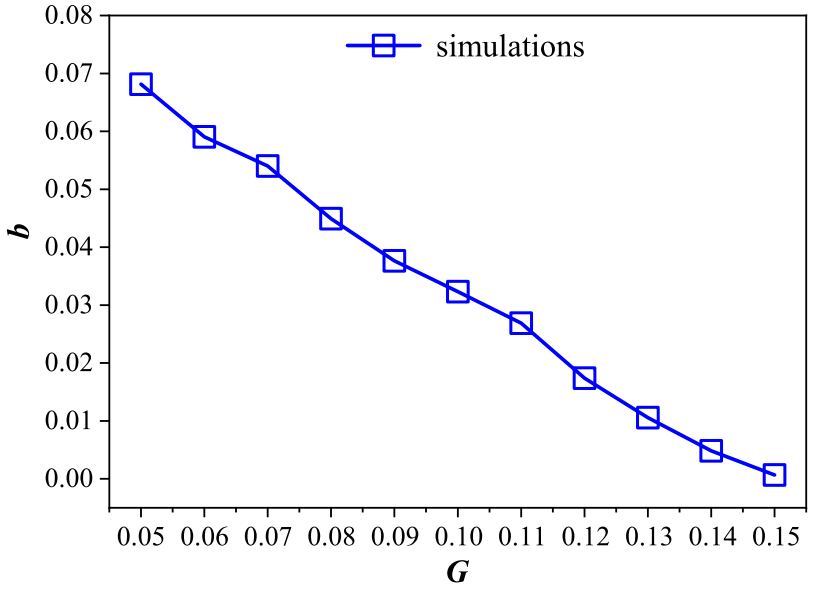


**Fig. 6.** The relationship between $b$ and $G$ from Eq. (11). The coupling strength $G$ is from 0.05 to 0.15 with interval 0.01.

Submitting Eq. (14) into Eq. (13), we have

$$\Omega_c \approx \omega - \frac{L^2}{R\sqrt{L^2 - b^2}} q_c. \tag{15}$$

From Eq. (11), we obtain that the relationship between $b$ and $G$ is shown in Fig. 6. It follows that $b$ decreases with the increase of G. Eq. (14) shows that the relationship of $q_c$ to $b$ is negative, therefore, $q_c$ increase with $G$ increase. Moreover, from Eq. (15), we observe that the relationship between $\Omega_c$ and $q_c$ is negative, i.e., the relationship between the critical free running period $FRP_c$ and $q_c$ is positive. Accordingly, $FRP_c$ increase with $G$ increase. In summary, we theoretically explain the results in Fig. 3.

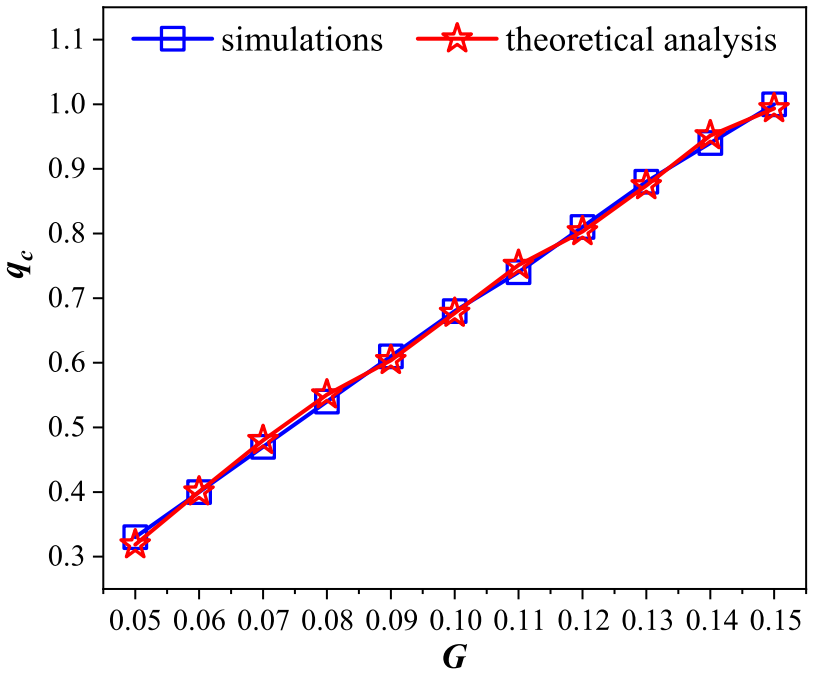


**Fig. 7.** The comparison in the relationship of $q_c$ to $G$ between the theoretical results and the numerical simulations. The coupling strength $G$ is from 0.05 to 0.15 with interval 0.01.

The comparison in the relationship of $q_c$ to $G$ between the theoretical results and the numerical simulations is shown in Fig. 7, and the theoretical results originate from Eq. (14) while the numerical simulations from Eq. (1). It is visible that the theoretical results are almost consistent with the numerical simulations.

## 5. Conclusion and discussion

In the present study, we examined whether the heterogeneity in the light-sensitivity of the SCN neurons affects the FRP based on the Poincaré model exposed to the constant light. From Aschoff's rule we know that light intensity increases the FRP in nocturnal animals [11]. However, rhythmic behavior in constant light is more complicated than the endogenous rhythms in constant darkness in rats [42–44]. In some rats, the SCN rhythm is robust because the SCN neurons are well synchronized, while other rats lose their rhythm. Our model shows that the FRP can be different between animals due to heterogeneity in the sensitivity to light for different subsets of neurons in the SCN. This is an extra potential mechanism for a longer FRP in constant light conditions among different animals and animal species.

Moreover, we found that there is a critical value in the heterogeneity degree. If the degree is smaller than the critical value, the neuronal periods of both subregions remain the same, which means that the SCN regions remain synchronized. The FRP increases if the degree of heterogeneity is higher. If the degree is larger than the critical value, the neuronal periods differ between subregions, where the periods of the VL neurons increase, while the periods of the DM neurons decrease with the increase of the degree, so the synchronization between these two subregions is lost. This critical value may be related to loss of rhythmicity that is experimentally found for some animals to appear in constant light conditions, while other animals continue to have a rhythm [45]. Some animals may have a higher degree of heterogeneity in light sensitivity than others, and may therefore become arrhythmic due to the loss of synchronization between both subregions, while other animals remain rhythmic because the subregions remain synchronized.

A possible reason for some animals to go above this critical value and become arrhythmic, and others to stay below this critical value and remain rhythmic may be explained by the difference in the period length of neurons between subregions in our model, i.e., the periods of the VL neurons are larger than those of the DM neurons. In future experiments it is worth examining whether the neurons that have a longer period may be more sensitive to light, while neurons that have shorter periods are less sensitive or even insensitive to light.

Another possibility is that some animals have a higher coupling $G$, while having the same sensitivity to light. With a higher coupling strength, the critical value where light sensitivity leads to arrhythmic behaviors is also higher, leading to the ability to remain rhythmic for a higher FRP.

It has been shown that the FRP can change in one animal in different photoperiods (seasons), or due to age [17,46]. For example, adolescents tend to have a longer chronotype, meaning having a longer FRP, than other age groups [46].

This change over time may also be related to either the neuronal endogenous periods in the different subregions leading to heterogeneous light sensitivity in VL and DM, or a change in the coupling strengths within the SCN.

Our findings help to understand the mechanisms that may be in play in constant light conditions, and explain how the effect of neuronal heterogeneity to light sensitivity affects the collective behavior of the SCN neurons. This helps to understand why some animals or animal species, including humans, have more difficulty adjusting their rhythms to the natural 24 h light-dark cycle than others.

## CRediT authorship contribution statement

**Jian Zhou:** Conceptualization, Methodology, Software, Formal analysis, Investigation, Data curation, Writing – original draft, Visualization. **Changgui Gu:** Formal analysis, Methodology, Validation, Resources, Writing – review & editing, Project, Administration, Funding acquisition, Supervision. **Bao Zhu:** Software, Visualization, Writing – original draft. **Huijie Yang:** Formal analysis, Methodology. **Jos H.T. Rohling:** Writing – original draft, Writing – review & editing.

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## Acknowledgments

This work is supported by the National Natural Science Foundation of China under Grant No. 11875042, Shanghai Natural Science Foundation of China under Grant No. 21ZR1443900 and the Shanghai project for construction of top disciplines, PR China under Grant No. USST-SYS01.

## Appendix A. Supplementary data

Supplementary material related to this article can be found online at https://doi.org/10.1016/j.cnsns.2022.106462.

Relationships of the FRP for each subregion to the heterogeneity degree $q$

Relationship of the FRP for each subregion in the small-world or completely random SCN network to the heterogeneity degree $q$

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