

Fast and Slow Lag Bands of Reciprocal Electro-cortical Connections Detected via a Quasi-Causal Measure



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Objectives:

- To characterize the timing of inter-regional neuronal transmission using ECoG data (exploratory).
- To apply a lagged quasi-causal measure and assess its statistical significance.
- To assess the *stability* of the measure's statistical significance.

Introduction

Electrocorticographic (ECoG) signals, acquired from consenting epilepsy patients for presurgical evaluation and functional mapping, provide a rare opportunity to study human brain electrical activity. ECoG functional connectivity measures (coherence, phase synchronization, Granger causality, etc.) quantify relational characteristics of large-scale brain networks, and may assist prediction of where or when a seizure begins. We employed a time-lagged information theoretic measure—linear quasi-causal conditional mutual information (lQCCMI, [1])—and robustly detected two distinct (fast and slow) lag bands for electrode pairs ranging 0.86 cm to 4.2 cm apart in an anterior temporal region.

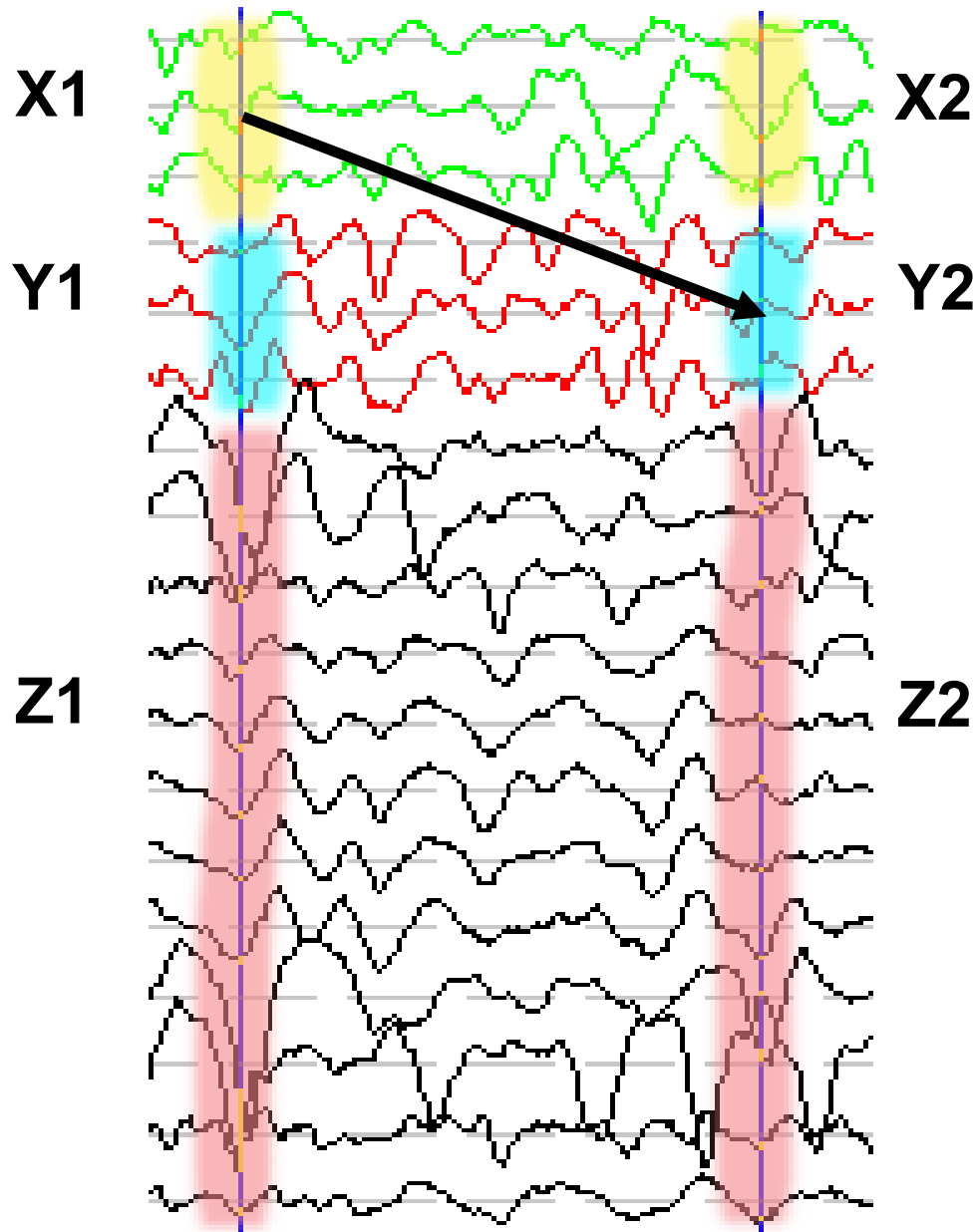


Figure 1. General setup for measuring lagged quasi-causal information from region X to region Y in the context of regions Z.

Quasi-causal conditional mutual information (QCCMI), is the mutual information between a region \mathbf{X} vector time series at an earlier time ($\mathbf{X1}$) and a region \mathbf{Y} vector time series at a lagged time ($\mathbf{Y2}$) conditional on \mathbf{Y} at the earlier time ($\mathbf{Y1}$), \mathbf{X} at the lagged time ($\mathbf{X2}$), and (optionally) the vector concatenation of other “context regions” \mathbf{Z} at both the earlier ($\mathbf{Z1}$) and lagged ($\mathbf{Z2}$) times.

Variant measures depend on how conditional mutual information is estimated (e.g., linear versus nonlinear estimators), whether time series are scalar or vector, and whether context regions are considered.

Methods

15-pairs analysis for 6 anterior temporal contacts (lags -125 ms to +125 ms) utilized ECoG (200 s at 400 Hz) filtered in three ways: 4-175 Hz (broad), 4-12.5 Hz (lower), and 12.5-175 Hz (upper). Minimum inter-sample duration was 500 ms (250 ms for upper) with average $N=296$ (592 for upper).

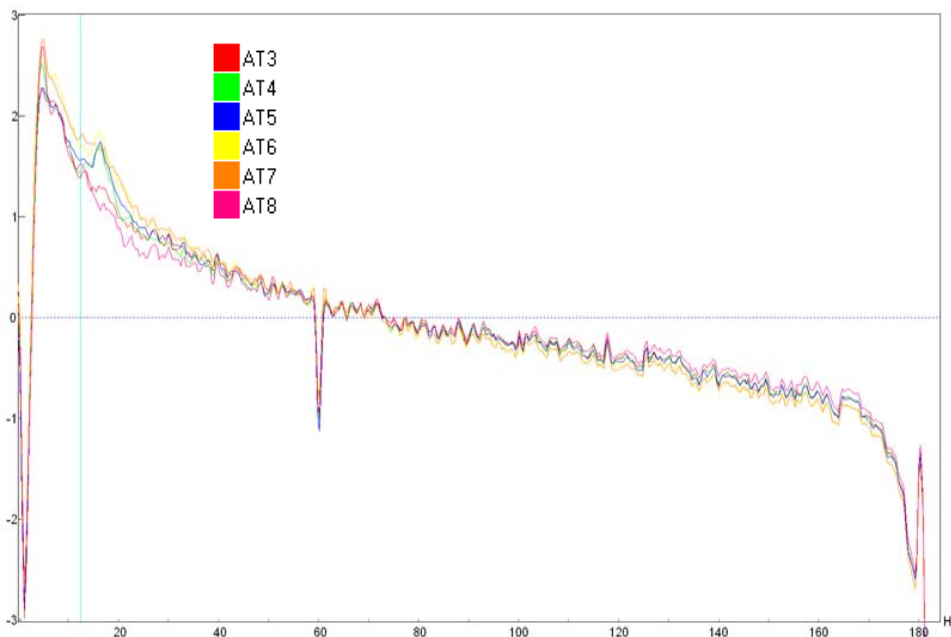


Figure 2. Log₁₀ power spectra estimated over 200 s, and adjusted so that the average between 4 Hz and 175 Hz is zero. Vertical blue line at 12.5 Hz. Fifth order 4-175 Hz bandpass filter and fourth order 60 Hz notch filter applied offline. Dynamic range: ~4 orders of magnitude.

Simple QCCMI measure:

- Linear estimator
- Scalar time series
- No context regions

Statistical significance. The *null distribution* of non-significant IQCCMI values is derived from a conditional independence distribution that preserves $p(\mathbf{x}(t), \mathbf{y}(t-\tau))$, $p(\mathbf{x}(t-\tau) | \mathbf{x}(t), \mathbf{y}(t-\tau))$, and $p(\mathbf{y}(t) | \mathbf{x}(t), \mathbf{y}(t-\tau))$, with enforced independence of the latter two densities. Thus, dependence between $\mathbf{x}(t-\tau)$ and $\mathbf{y}(t)$ is strictly conditional on the confounds. The null distribution is obtained by repeating (R times) the IQCCMI computation from N samples drawn independently from the conditional independence distribution. Thereby, a p-value is obtained that reflects statistical significance of the observed IQCCMI value. Average log p-values and their standard errors (reflecting statistical stability) are obtained by repeating (M times) the selection of N ECoG samples.

Results

Figures 3, 8, and 13 depict results for all region pairs, both directions, and the three filtering conditions (broadband, lowpass, and highpass).

Remaining figures enlarge the bidirectional results for four selected region pairs: AT5 and AT6 (Figures 4, 9, 13); AT4 and AT6 (Figures 5, 10, 15); AT3 and AT6 (Figures 6, 11, 16); and AT7 and AT8 (Figures 7, 12, 17).

In brief: For broad frequencies, statistically significant ($p < 0.05$) and stable ($se < 0.005$) quasi-causal effects were detected for all pairs in two nearly symmetric lag bands: fast (8.5-24 ms) and slow (70-109 ms). Lower frequency effects were very roughly similar. Upper frequency effects were restricted to 5 pairs, all of which exhibited 5 distinct and symmetric lag bands.

Conclusions

- Statistically significant ($p < 0.05$) lagged IQCCMI results were stable ($se < 0.005$) for 200 s of data.
- Separate fast and slow transmission pathways may coexist reciprocally between nearby cortical areas.
 - Fast and slow lag bands, which would correspond roughly to 21-59 Hz and 4.6-7.1 Hz recycling oscillations, were not associated simply with upper and lower ECoG frequencies.
 - Lower frequency influences were detected pervasively.
 - Upper frequency influences, when detected, showed more detailed lag structure, which was highly symmetric.

Questions for further study

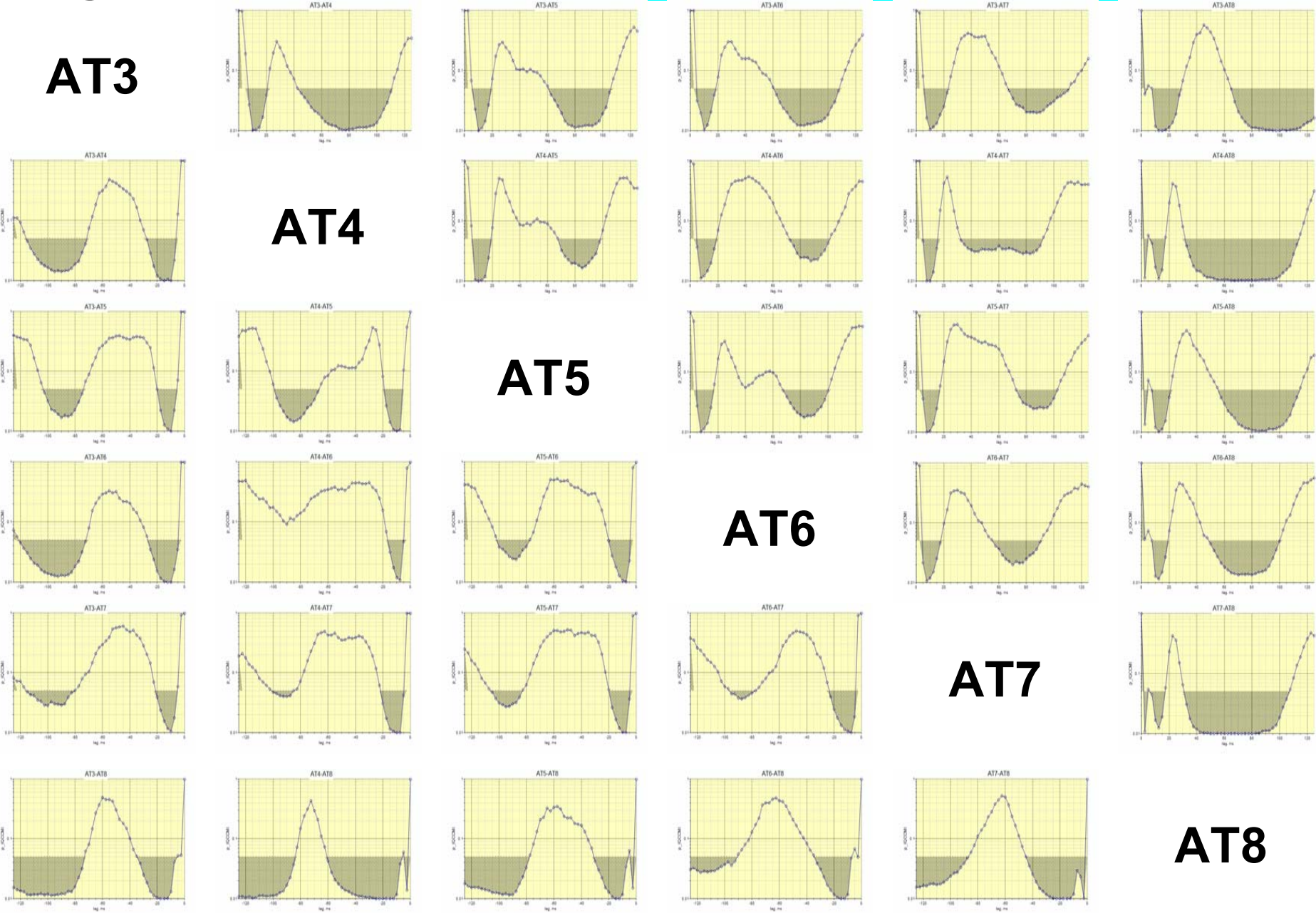
- *How do results depend on QCCMI variants?*
 - Inclusion of context regions
 - *Lag bands more specific?*
 - Vector time series (e.g., embedding or SSA)
 - Nonlinear estimator for conditional mutual information
- Upper and lower frequencies apparently are not independent with respect to influences from one region to another. *How and why do upper and lower frequency bands interact?*
- Most results were symmetric, although some were highly asymmetric (e.g., AT4-AT6 broadband and lowpass; AT7-AT8 broadband and lowpass). *Does asymmetry have possible clinical significance for epilepsy?*

Reference

[1] Pflieger ME, Greenblatt RE. Using conditional mutual information to approximate causality for multivariate physiological time series. *Int J Biomagnetism* 2005; 7(2): 285-8.

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Fig. 3. Lag p-values for BROADBAND (4-175 Hz) data



AT5-AT6 Broadband (4-175 Hz)

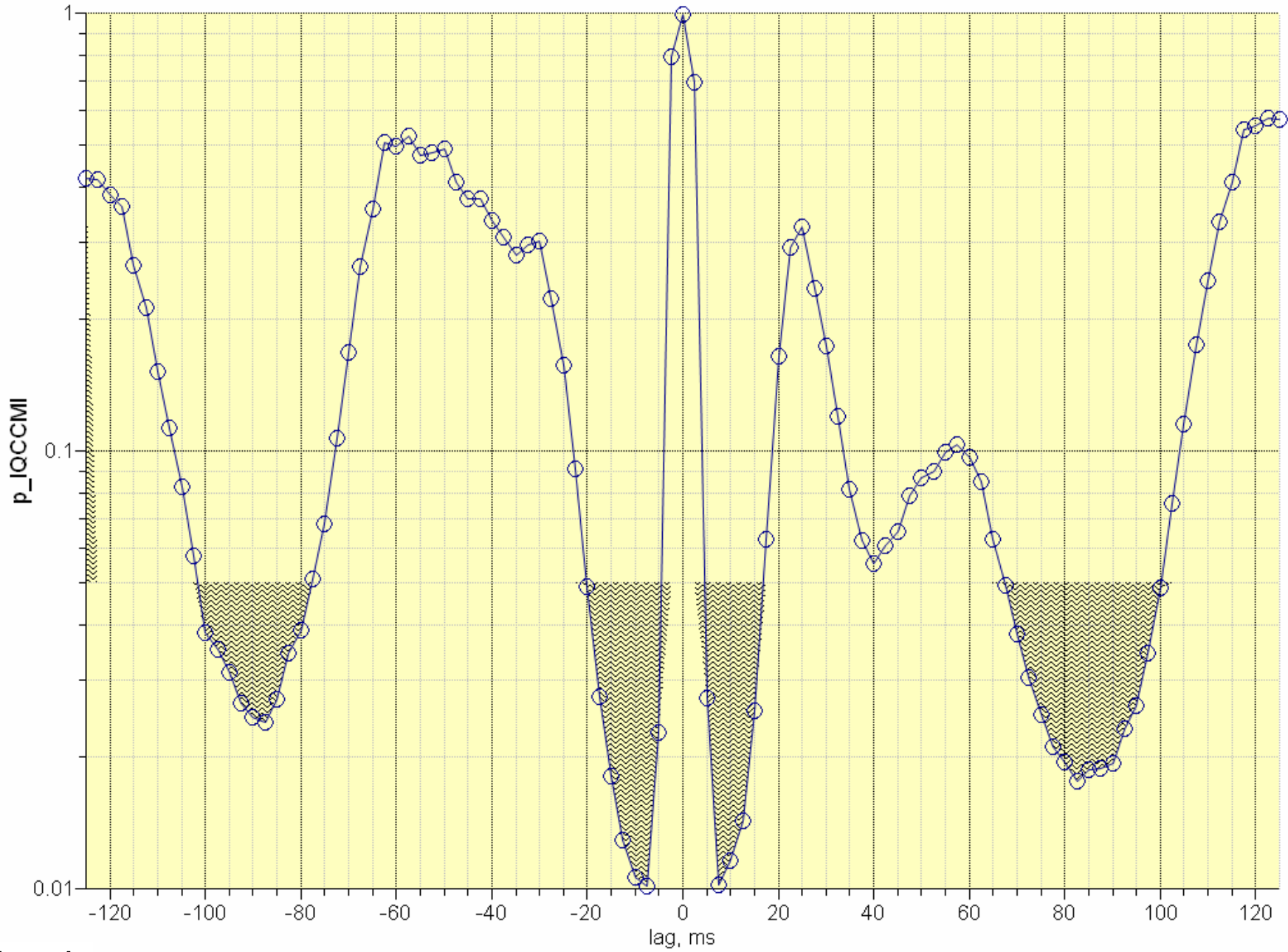


Fig. 4

AT4-AT6 Broadband (4-175 Hz)

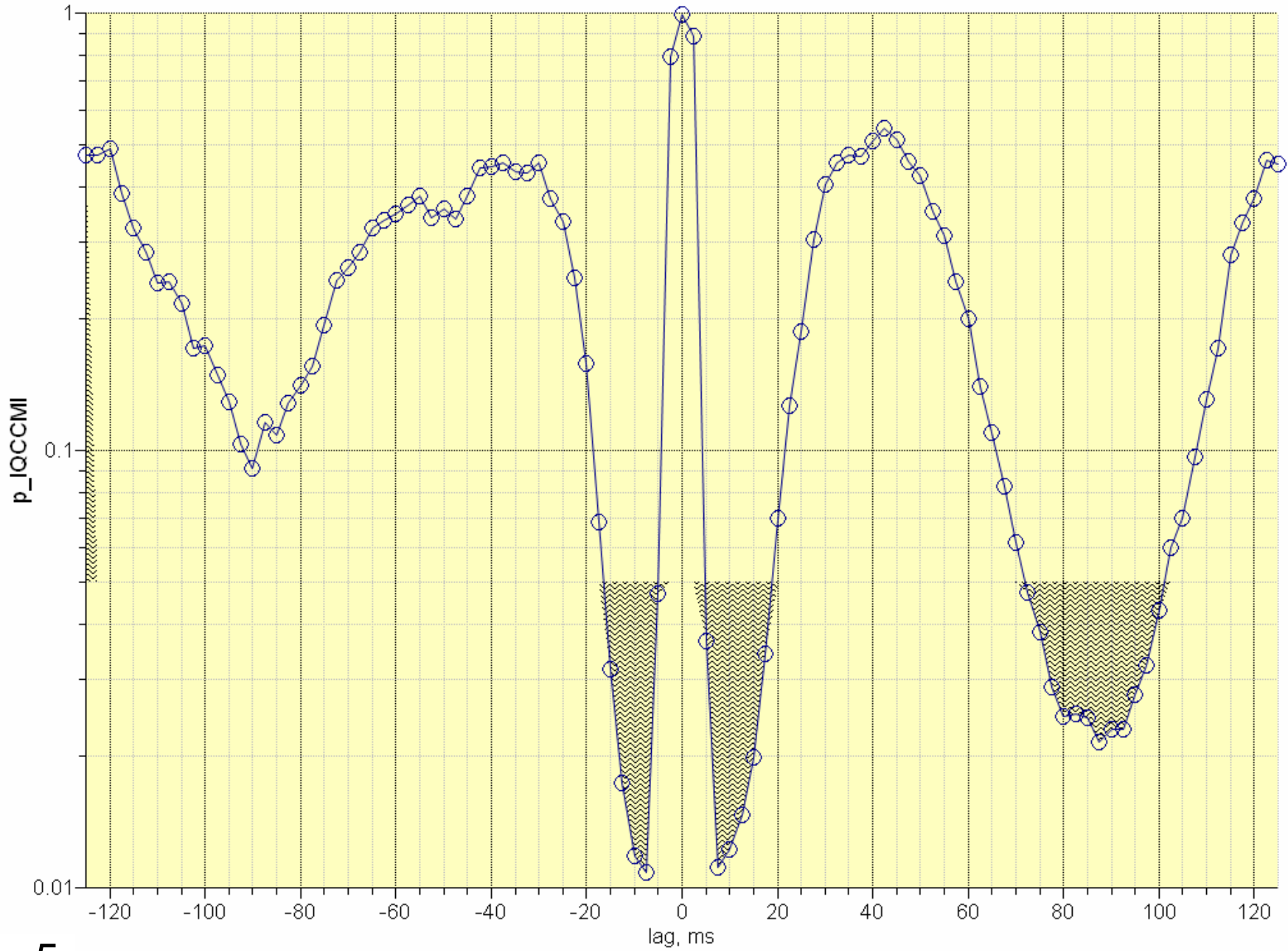


Fig. 5

AT3-AT6 Broadband (4-175 Hz)

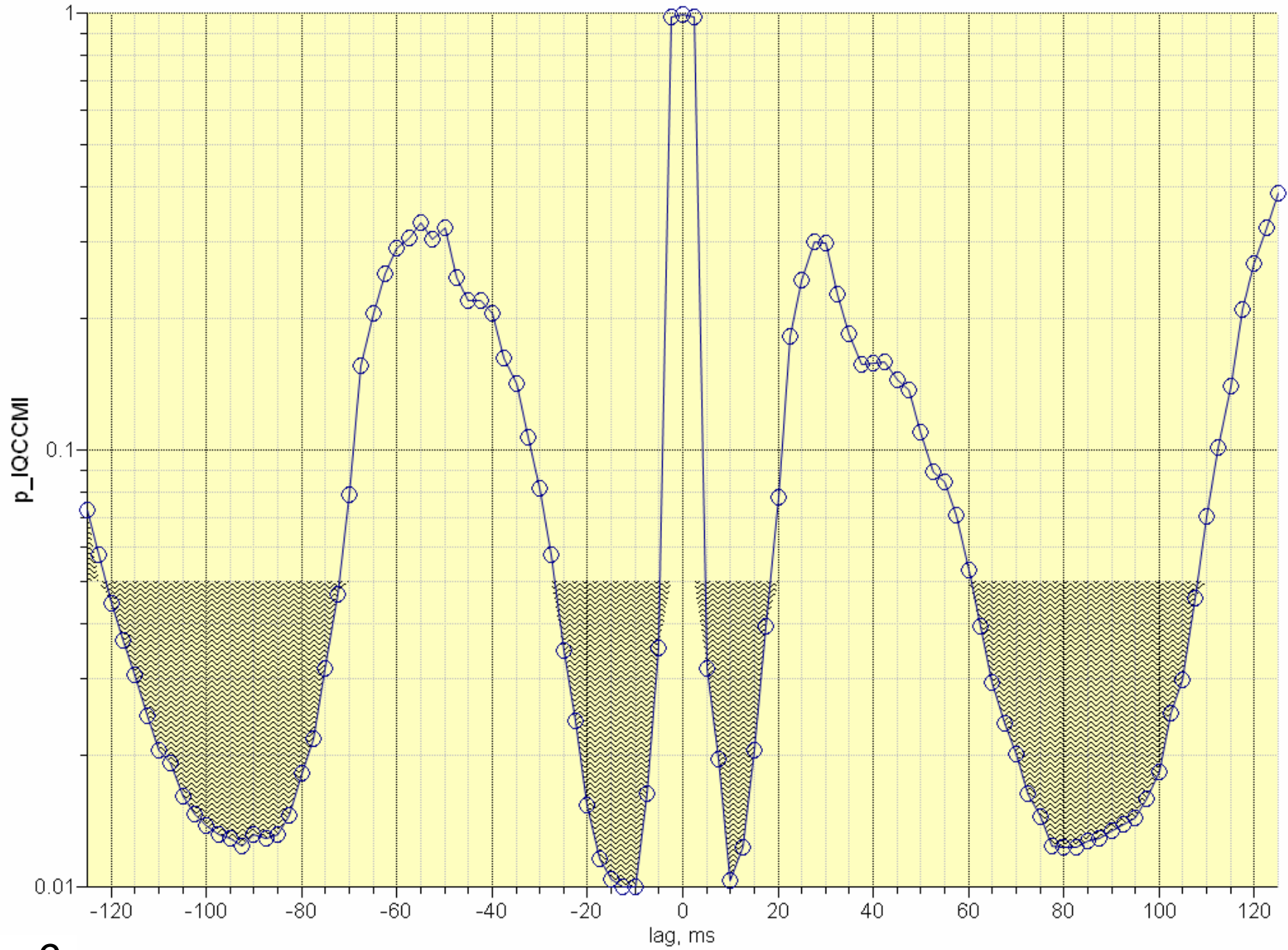


Fig. 6

AT7-AT8 Broadband (4-175 Hz)

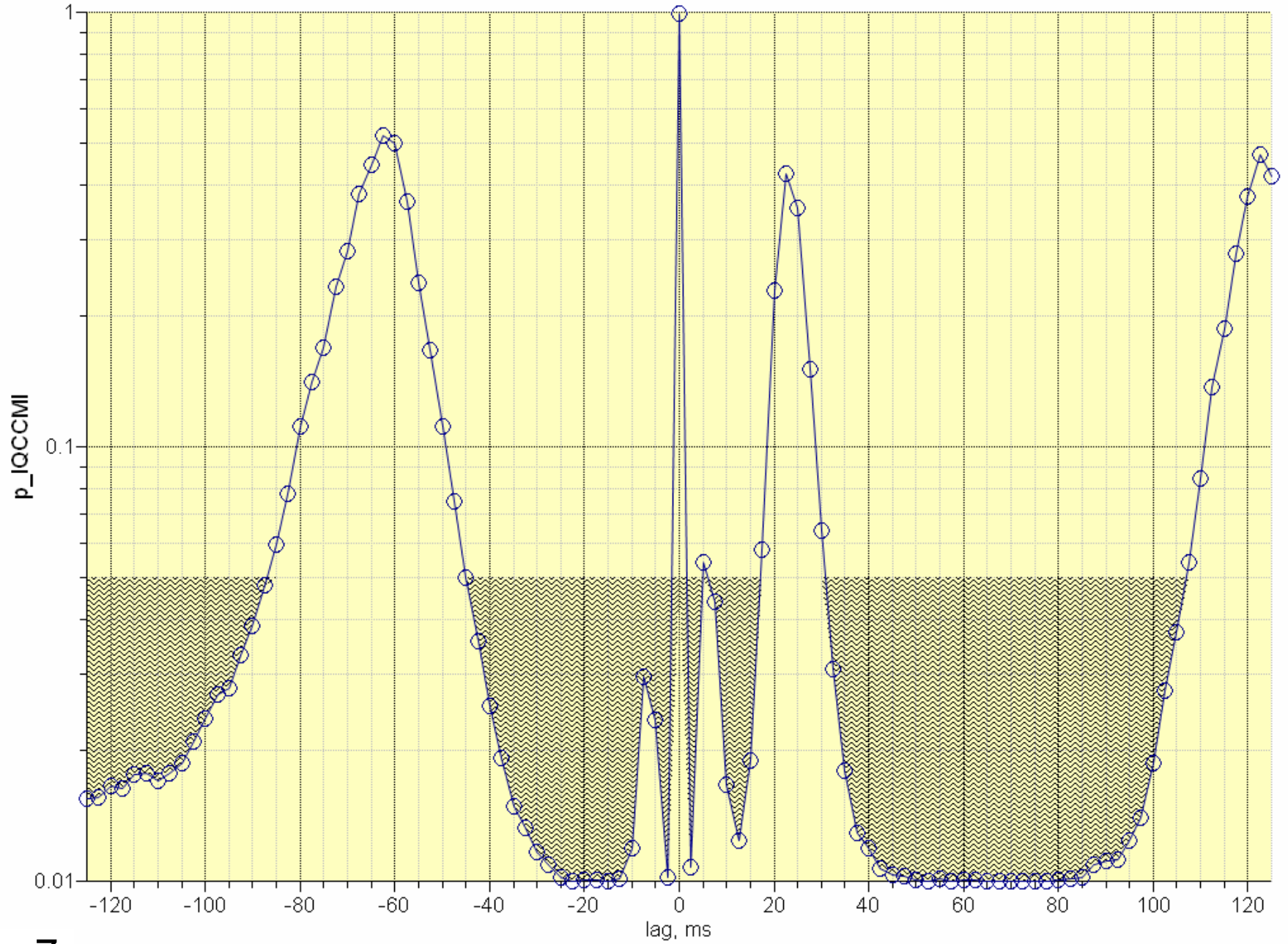
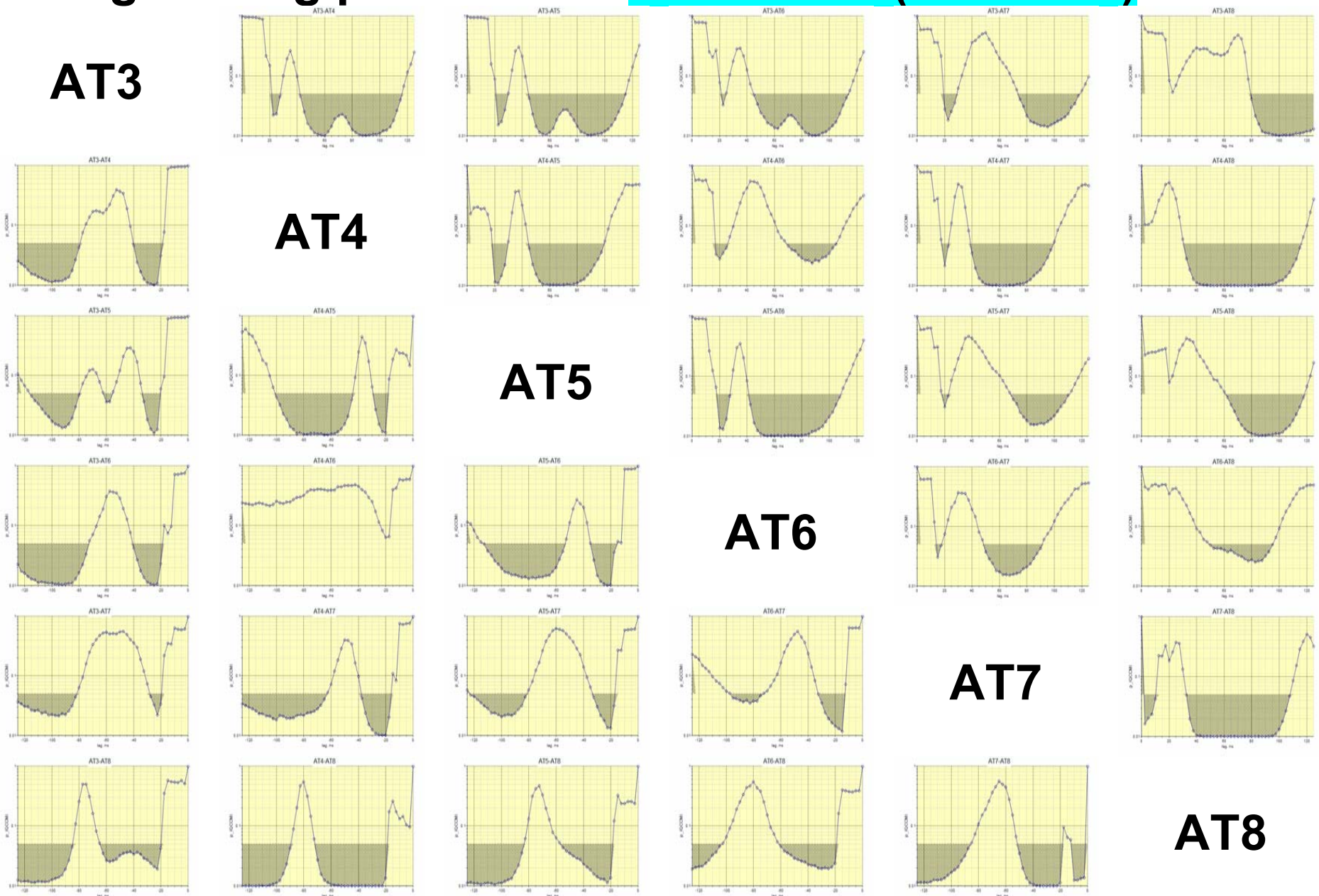


Fig. 7

Fig. 8. Lag p-values for LOWPASS (4-12.5 Hz) data



AT5-AT6 Lowpass (12.5 Hz)

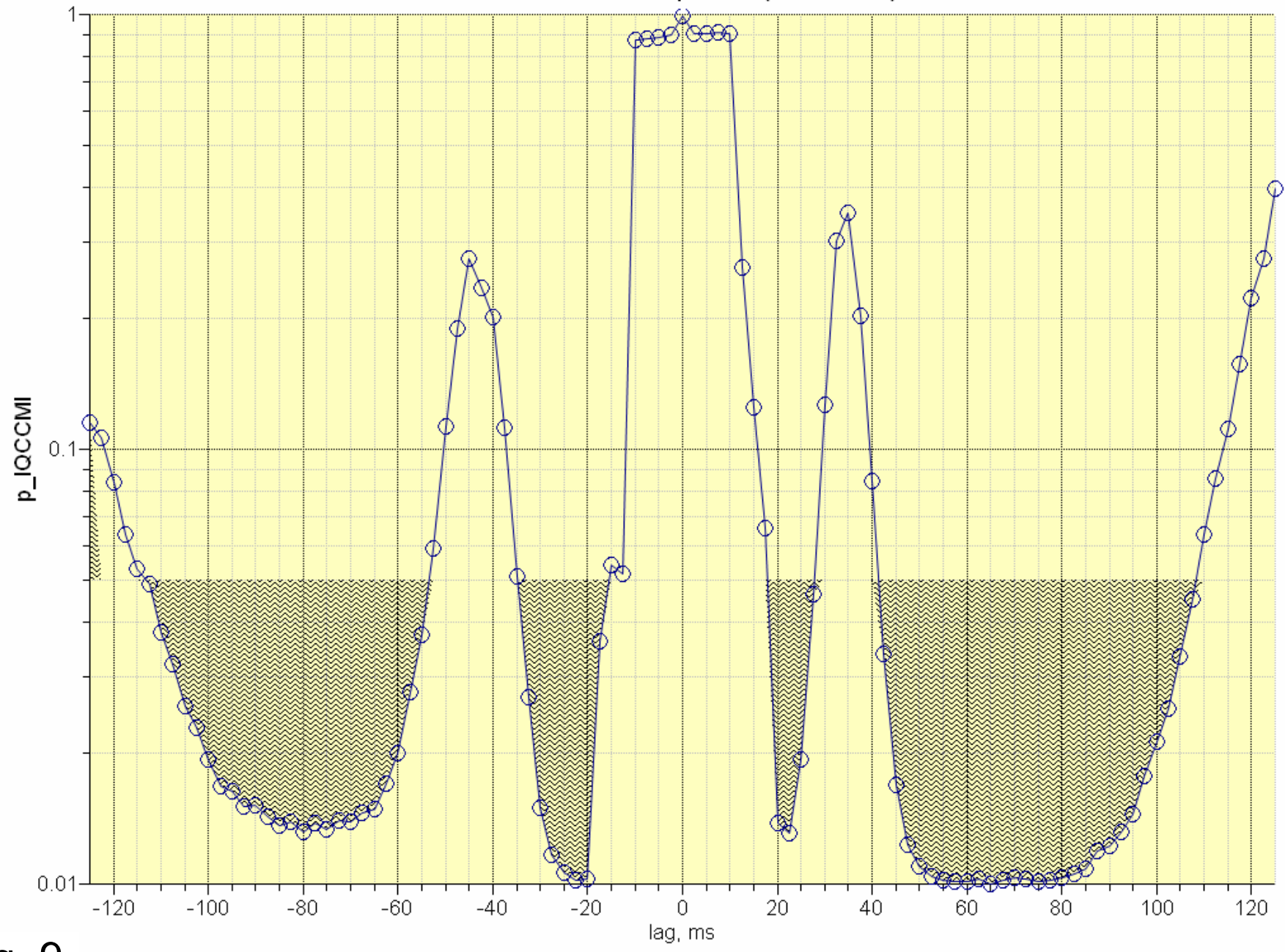


Fig. 9

AT4-AT6 Lowpass (12.5 Hz)

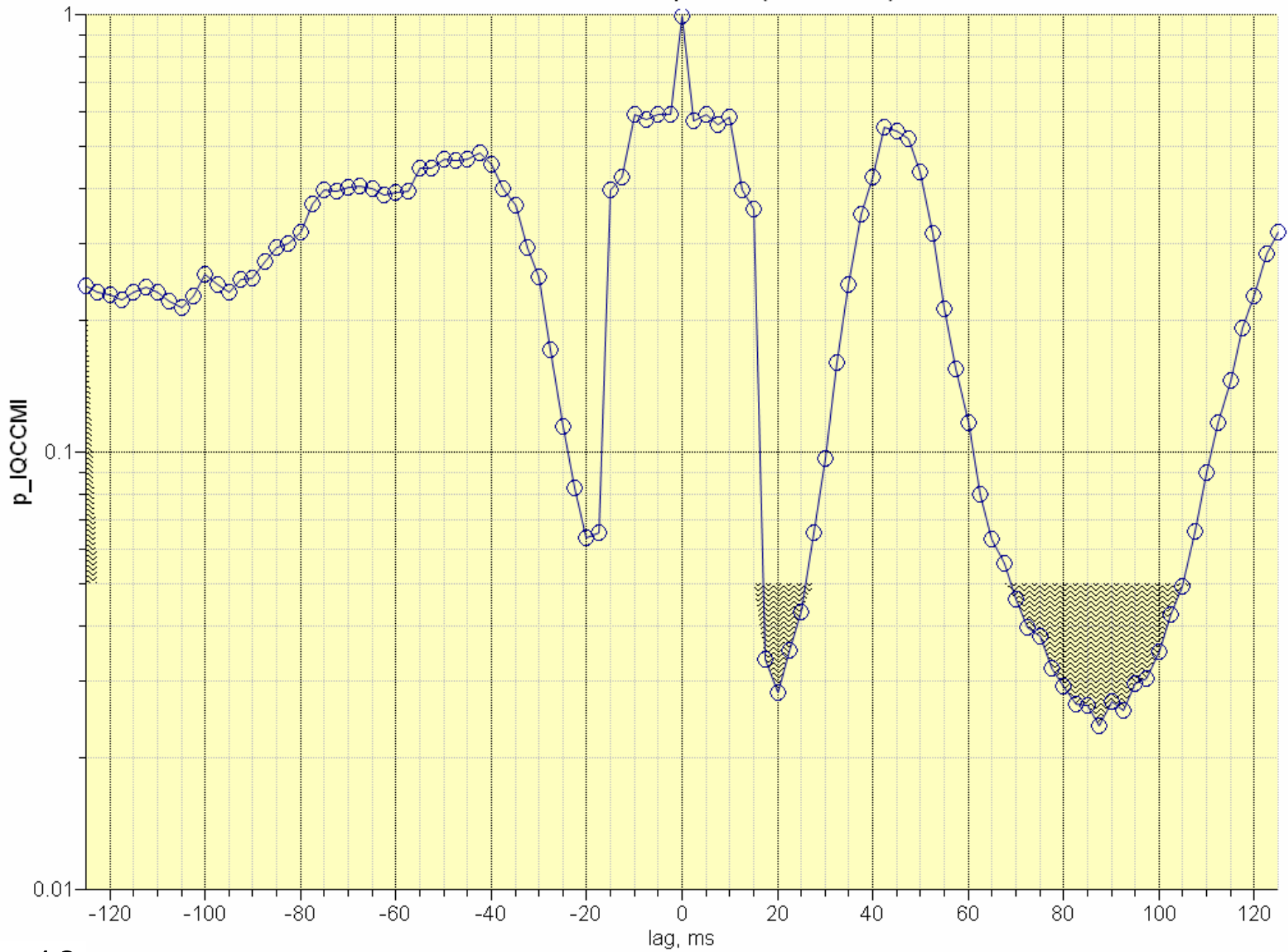


Fig. 10

AT3-AT6 Lowpass (12.5 Hz)

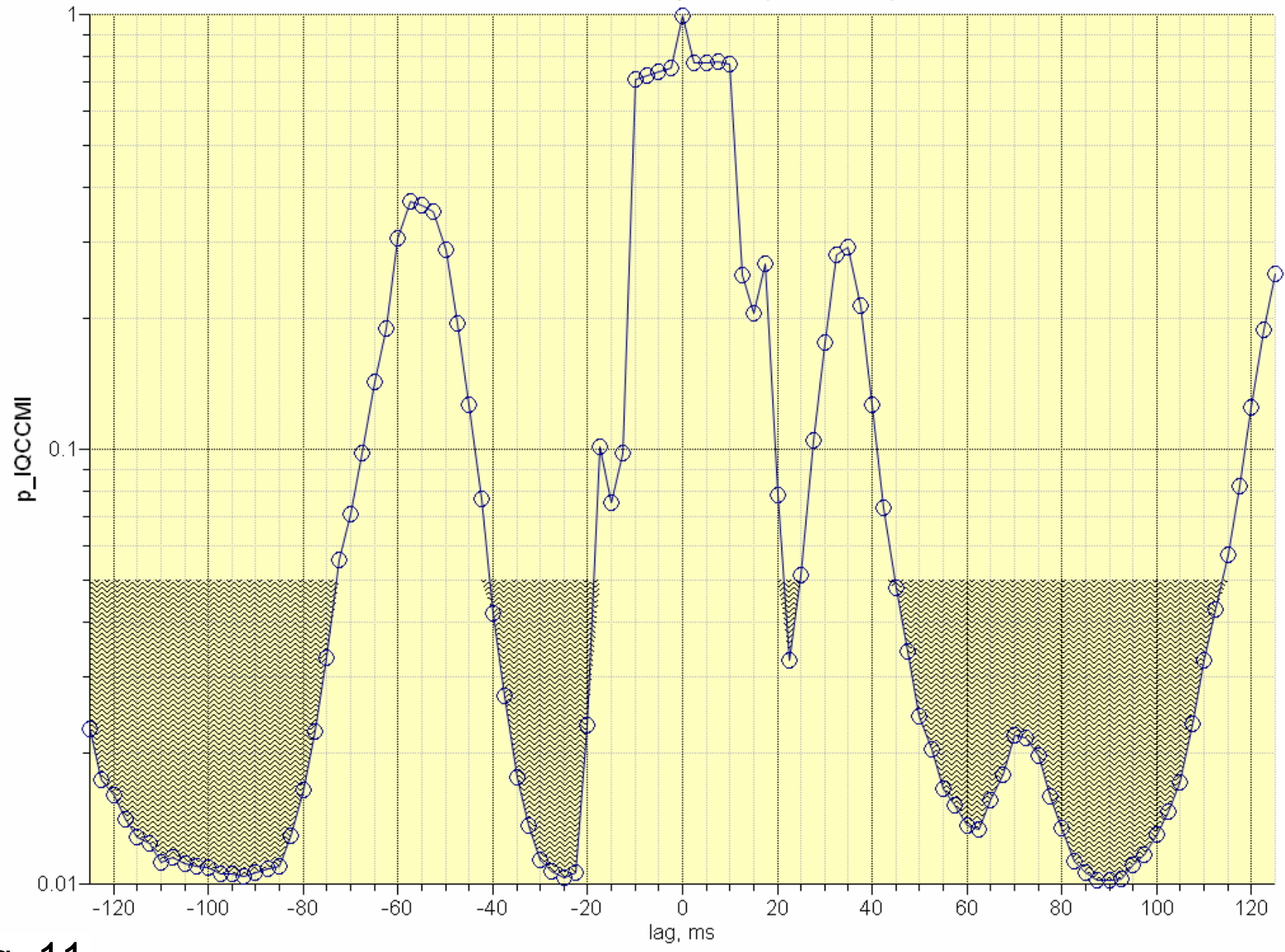


Fig. 11

AT7-AT8 Lowpass (12.5 Hz)

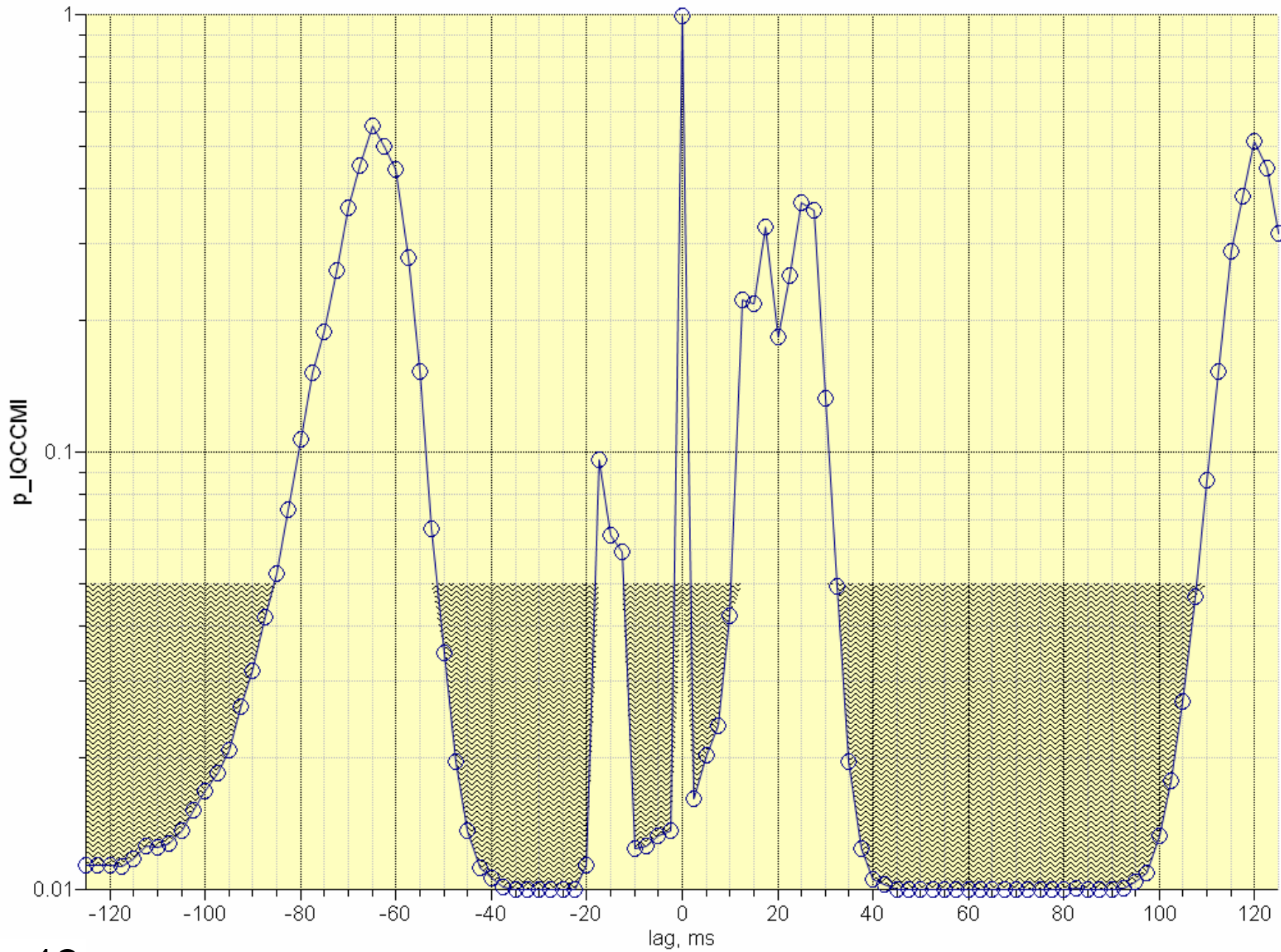
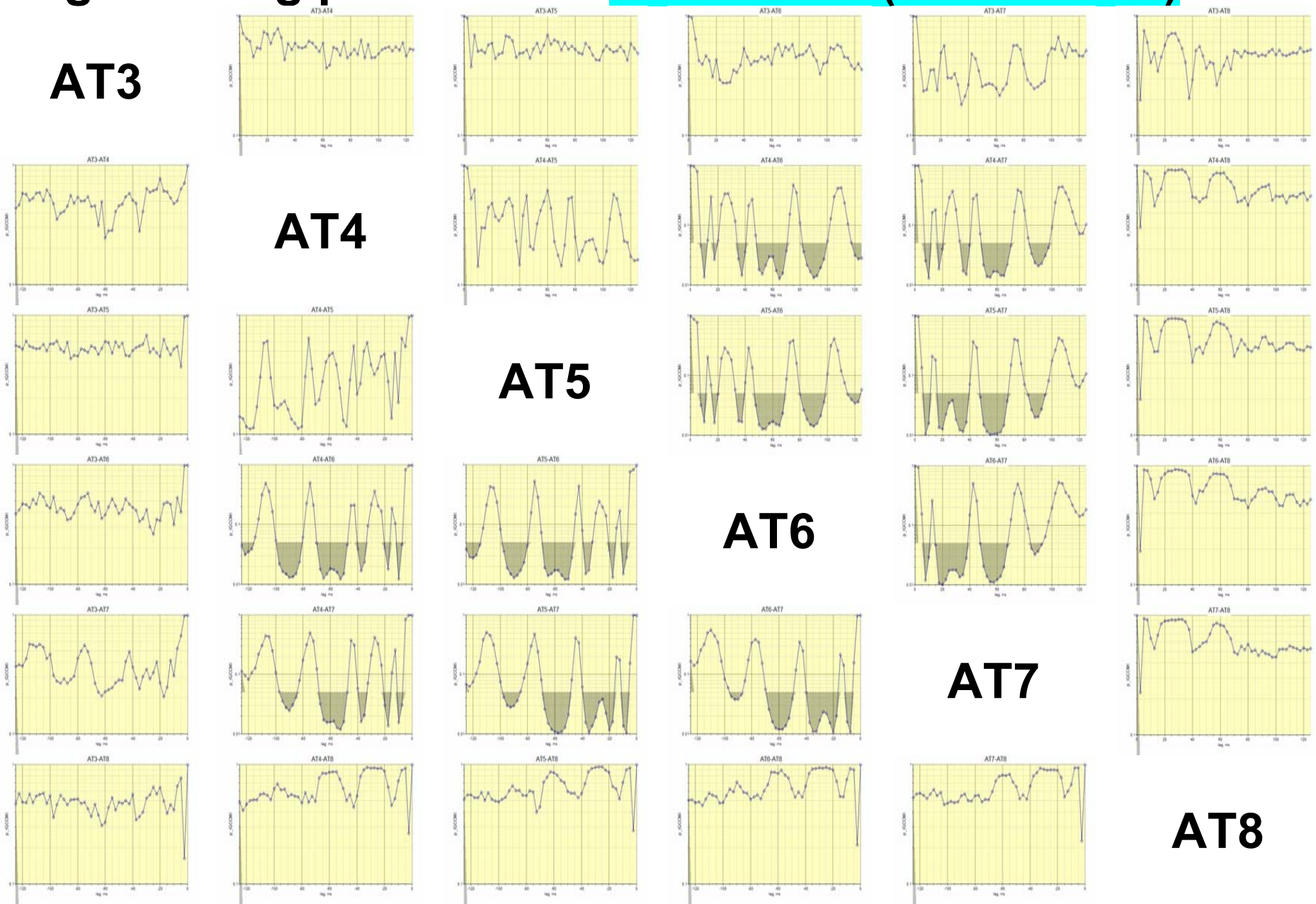


Fig. 12

Fig. 13. Lag p-values for HIGHPASS (12.5-175 Hz) data



Note: Ordinates for shaded graphs log-scaled from 0.01 to 1.0. All other graphs scaled from 0.1 to 1.0.

AT5-AT6 Highpass (12.5 Hz)

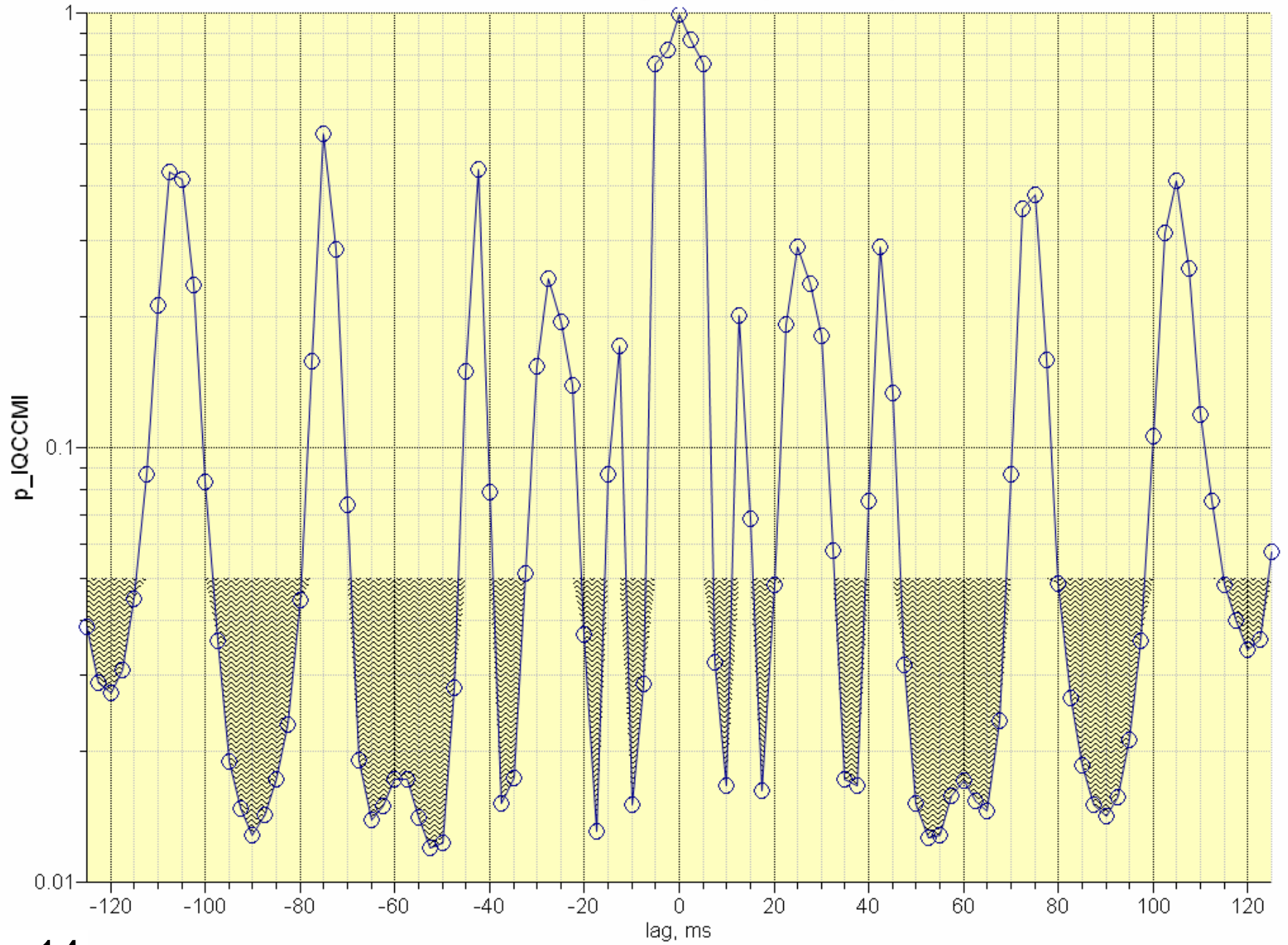


Fig. 14

AT4-AT6 Highpass (12.5 Hz)

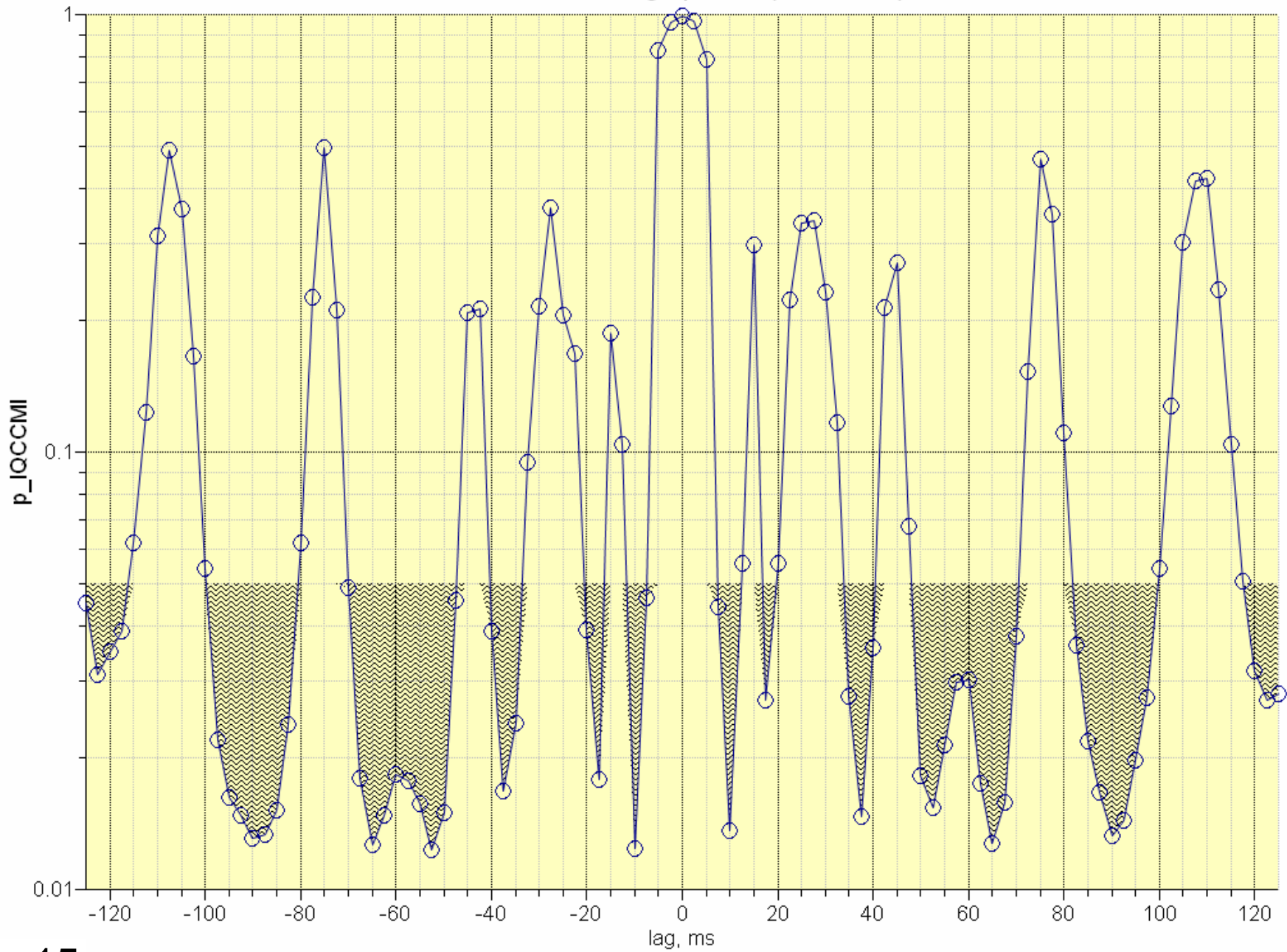


Fig. 15

AT3-AT6 Highpass (12.5 Hz)

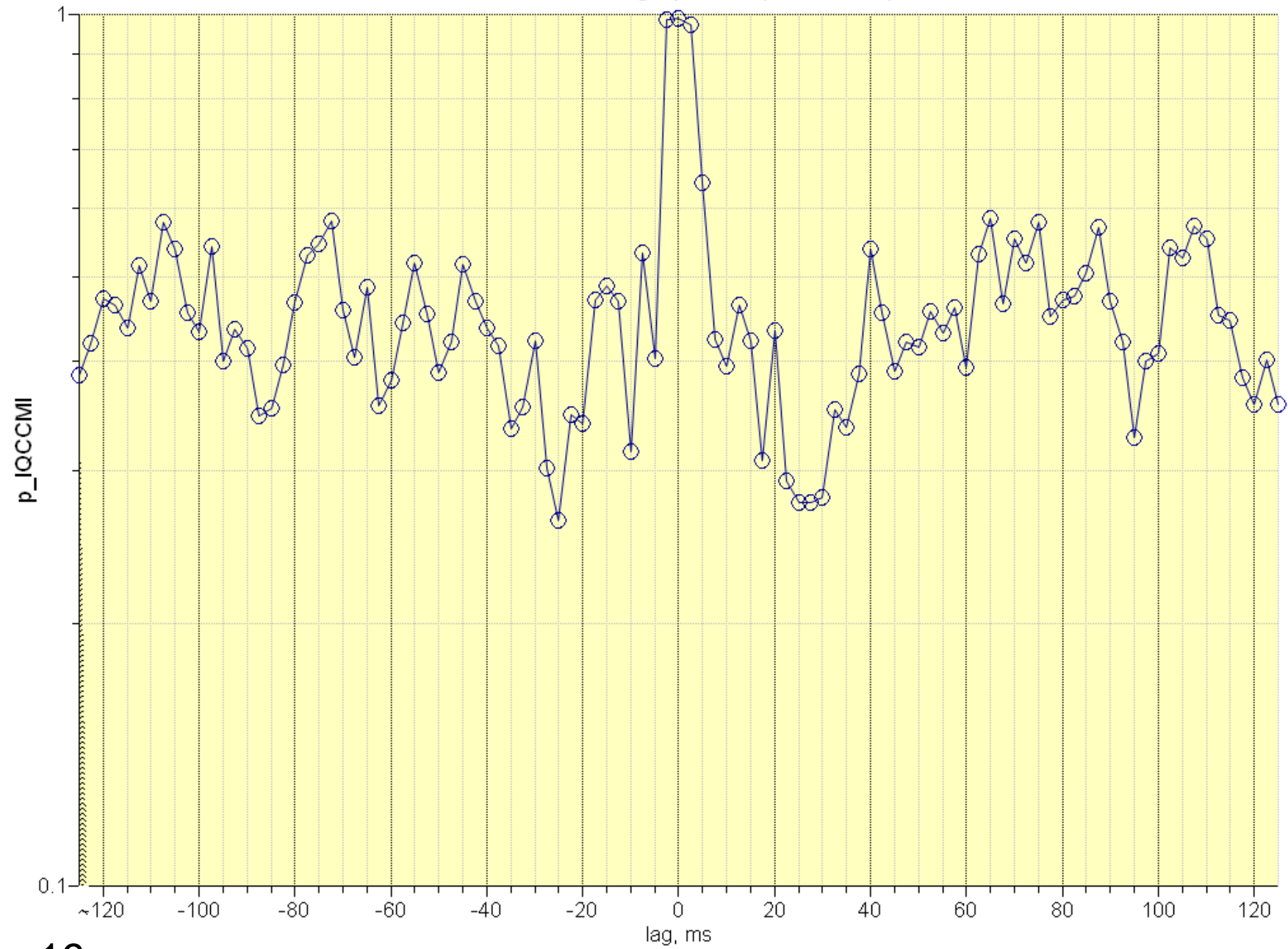


Fig. 16

AT7-AT8 Highpass (12.5 Hz)

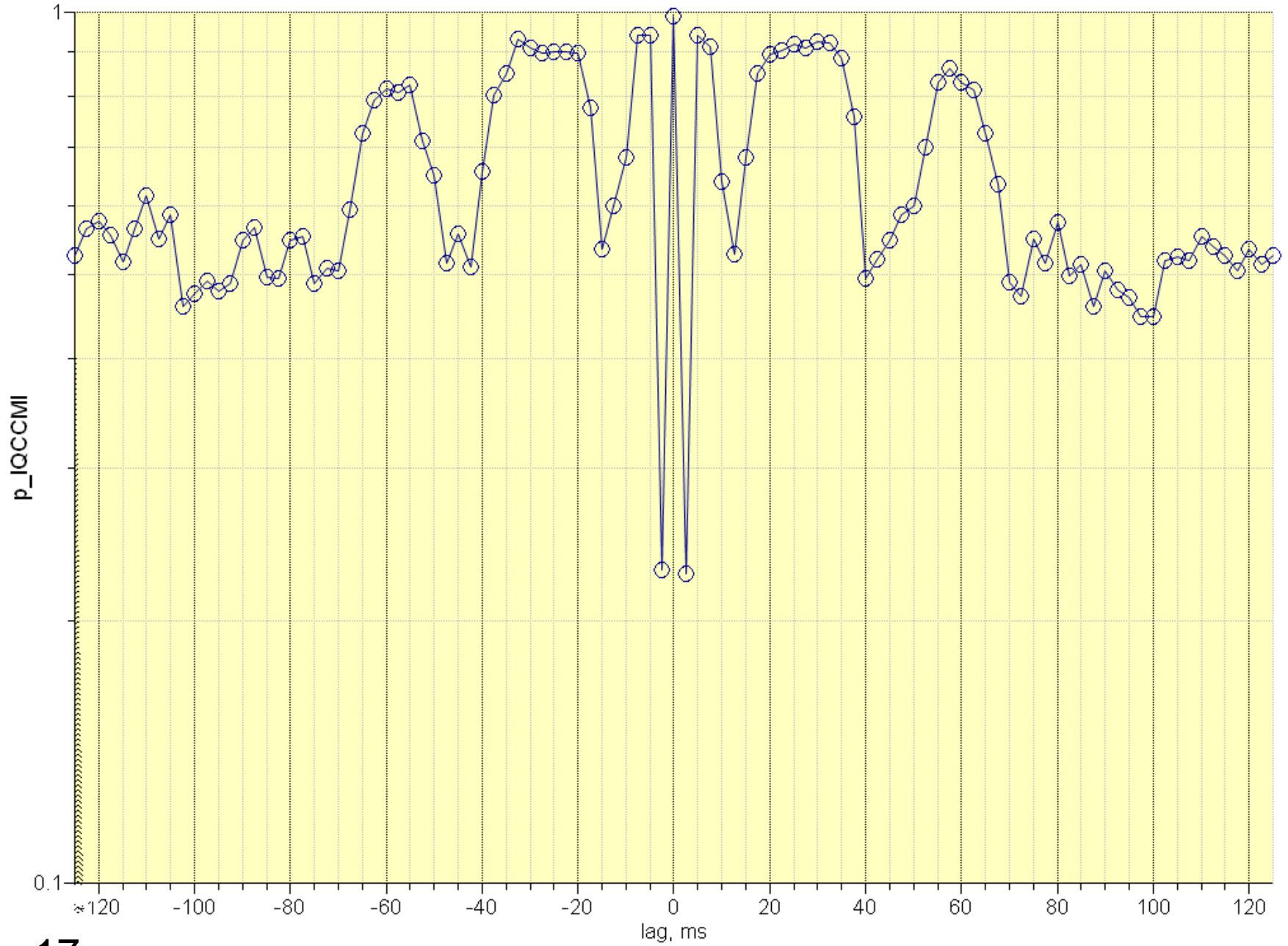


Fig. 17